Cardiovascular Embryology

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Embryology of the Vascular System

- EARLY DEVELOPMENT OF EMBRYO
- ESTABLISHMENT OF THE CARDIOGENIC FIELD
- FORMATION AND POSITION OF THE HEART TUBE
- FORMATION OF THE CARDIAC LOOP
- MOLECULAR REGULATION OF CARDIAC DEVELOPMENT
- DEVELOPMENT OF THE SINUS VENOSUS
- FORMATION OF THE CARDIAC SEPTAE
- FORMATION OF THE CONDUCTING SYSTEM OF THE HEART
- VASCULAR DEVELOPMENT

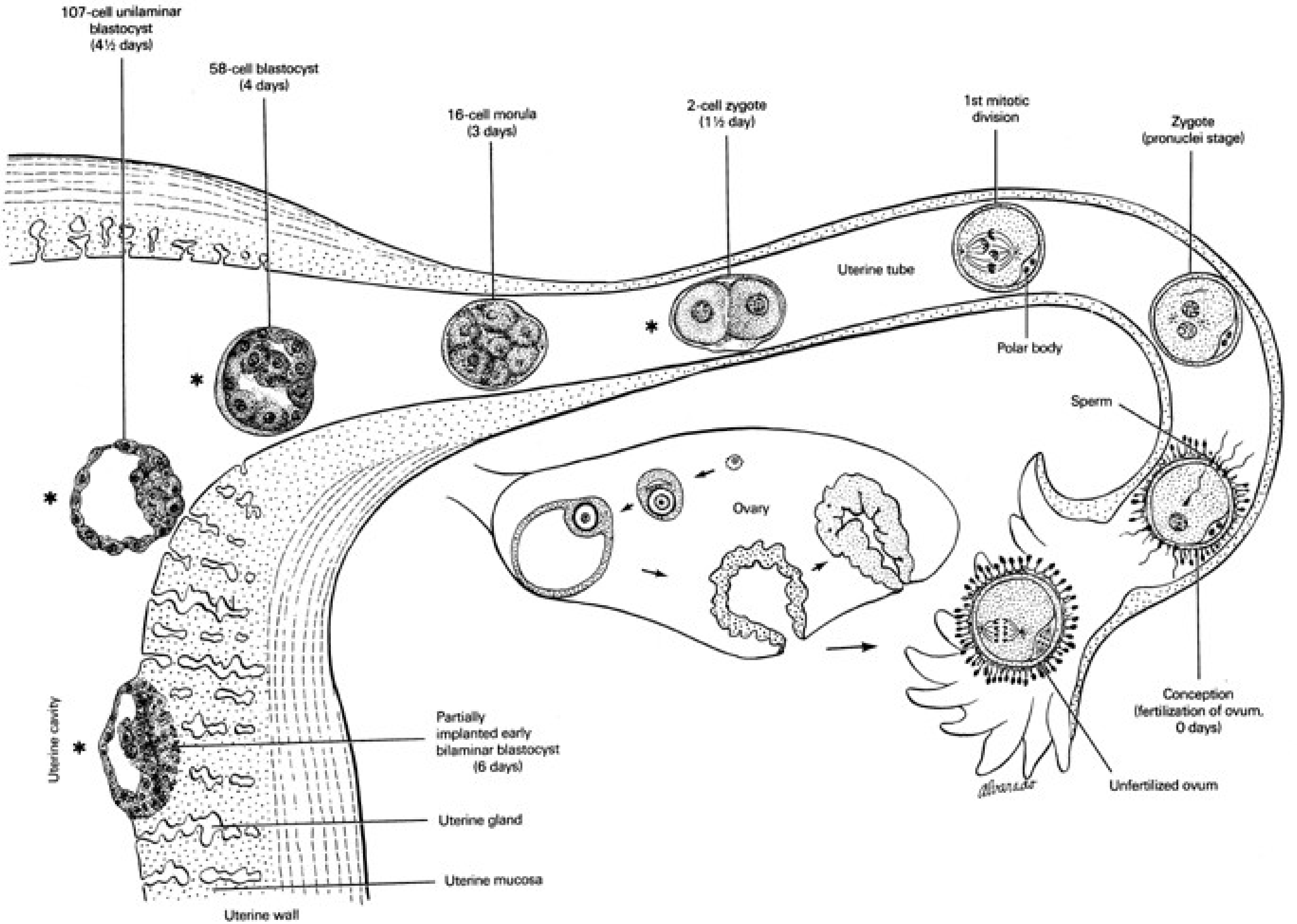
Early Development Of Embryo

Chronology of events

- Day 0 – **fertilization** and initiation of embryogenesis
- Week 1 – **blastocyst** formation and **implantation**
- Week 2 – formation of **bilaminar germ disc** (epiblast and hypoblast)
- Week3 – formation of **trilaminar germ disc** (gastrulation)
- Mid week 3 – **heart** begins to form
- Week 4 – **cardiac looping** begins
- Mid week 4 – development of **sinus venosus**
- Week 4-5 – development of **cardiac septae**, development of **aortic arches,** development of **arterial and venous system** beg

1st week of development

- Day 0 – fertilization
- Day 1 – zygote formation
- Day 2 – 2 cell stage (30 hrs)
- Day 2 – 4 cell stage (40 hrs)
- Day 3 – 16 cell stage
- Day 4 – morula (32 cell stage)
- Day 5 – blastocyst (inner cell mass-embryoblast and outer cell mass-trophoblast)
- Day 6 – implantation



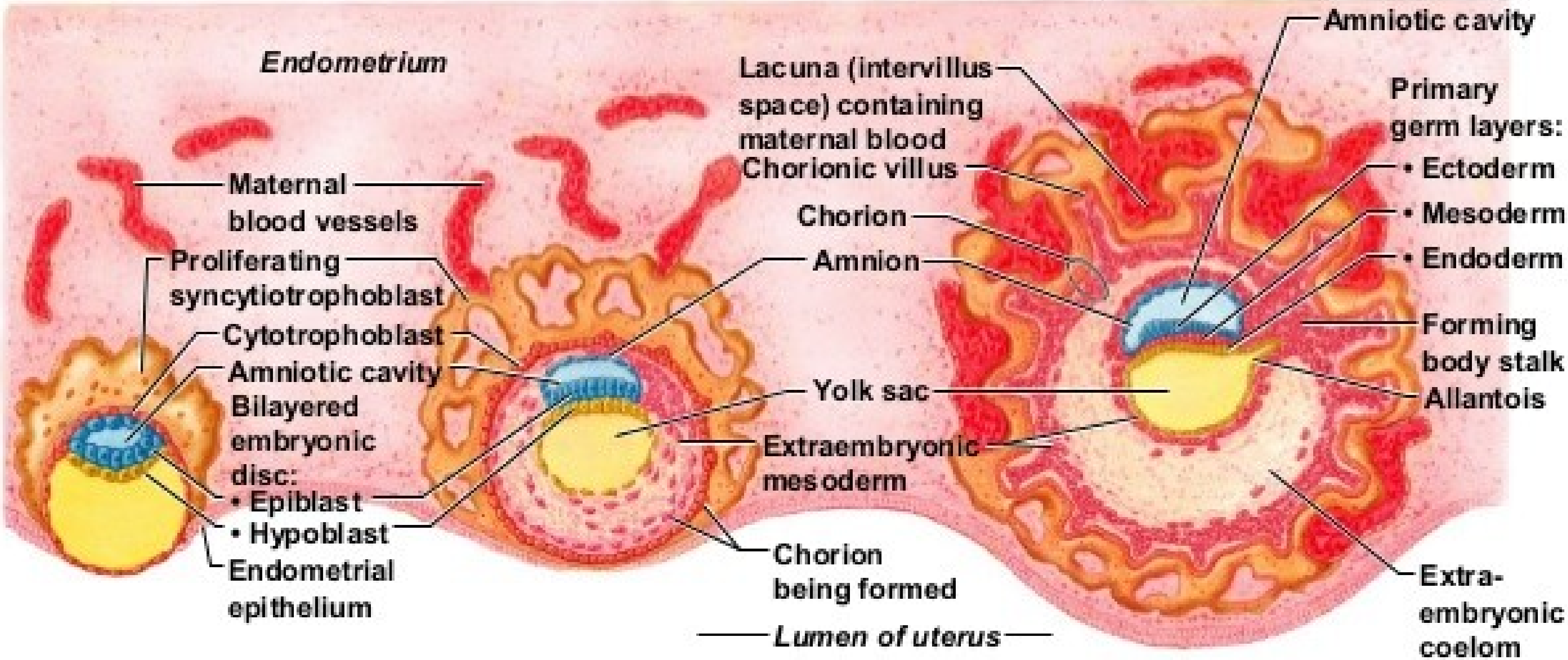
107-cell unilaminar blastocyst (4½ days)
58-cell blastocyst (4 days)
16-cell morula (3 days)
2-cell zygote (1½ day)
1st mitotic division
Zygote (pronuclei stage)
Uterine tube
Polar body
Sperm
Ovary
Conception (fertilization of ovum, 0 days)
Unfertilized ovum
Partially implanted early bilaminar blastocyst (6 days)
Uterine cavity
Uterine gland
Uterine mucosa
Uterine wall

2 Week of development

Week of **TWO**s:

- The trophoblast differentiates into 2 layers,
  - cytotrophoblast
  - Syncytiotrophoblast
- The embryoblast forms 2 layers,
  - epiblast
  - hypoblast.
- The extraembryonic mesoderm splits into 2 layers,
  - Somatopleural
  - splanchnopleural
- 2 cavities,
  - amniotic cavity
  - yolk sac cavity
- Beginning of uteroplacental circulation

Events of placentation, early embryonic development, and extraembryonic membrane formation



(a) $7\frac{1}{2}$-day implanting blastocyst

(b) 12-day implanted blastocyst

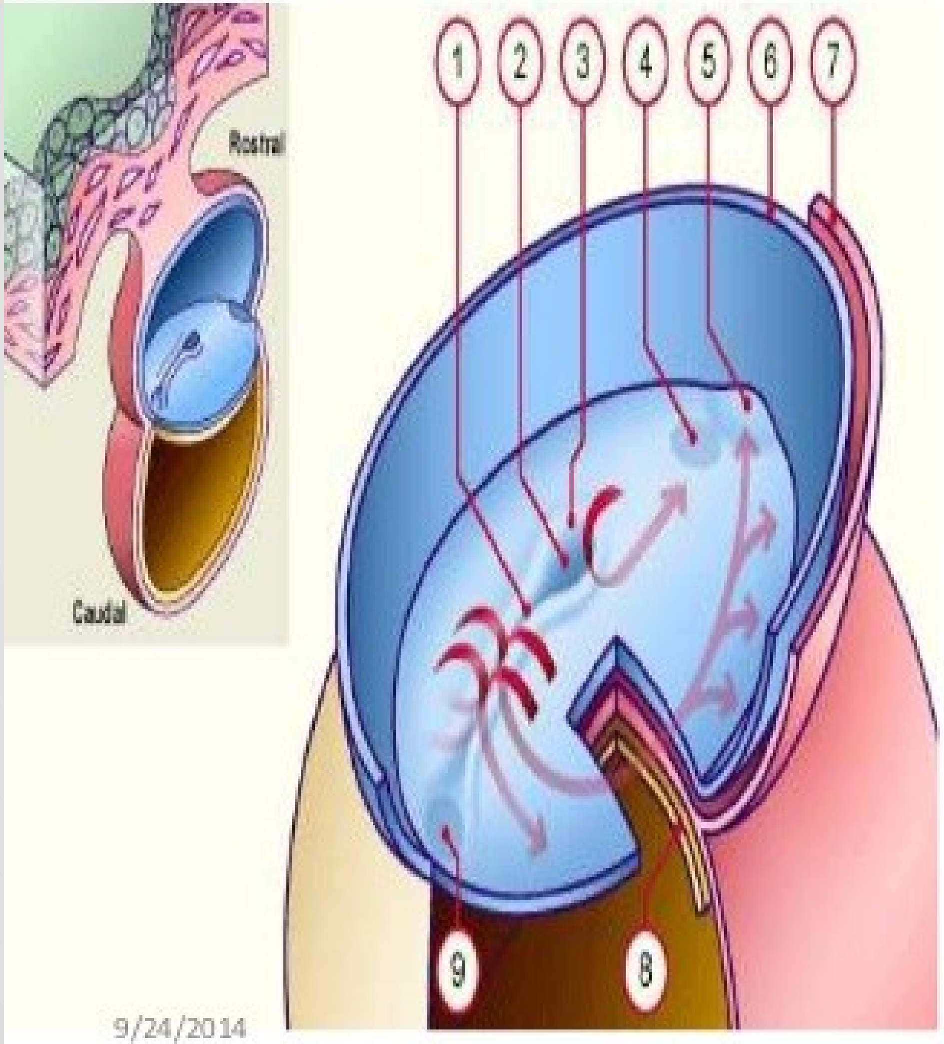
(c) 16-day embryo

Human Anatomy and Physiology, 7e
by Elaine Marieb & Katja Hoehn

3^{rd} week of development

- Formation of trilaminar germ disc (Gastrulation)
  - Ectoderm
  - Mesoderm
  - Endoderm
- Appearance of primitive streak
- Formation of notochord
- Formation of oropharyngeal and cloacal menbrane
- Establishment of body axes
- Further development of trophoblast – appearance of tertiary chorionic villi

The embryonic disk 3rd week of I.U.L.



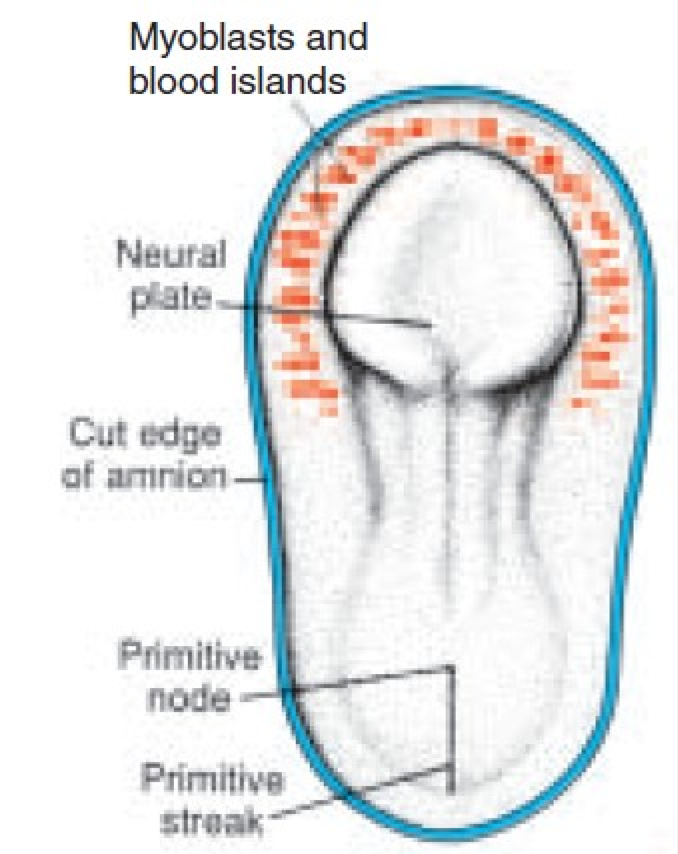
- 1. Primitive groove
- 2. Primitive pit
- 3. Primitive node
- 4. Oropharyngeal membrane
- 5. Cardial plate
- 6. Sectional edge of amniotic membrane
- 7. Mesoderm
- .
- 8. Endoderm
- 9. Future cloacal membrane
- NB -1+2+3 primitive streak

Cardiac Embryogenesis

ESTABLISHMENT OF THE CARDIOGENIC FIELD

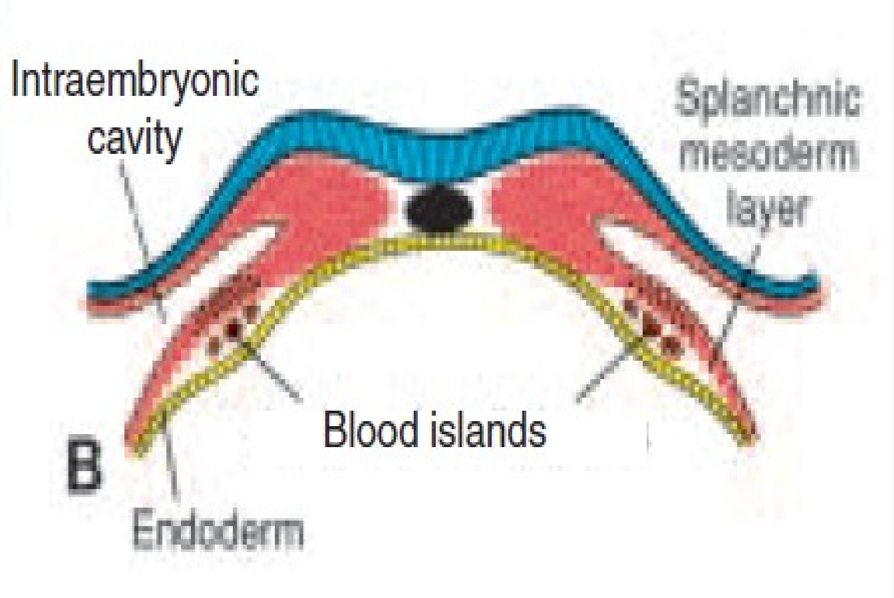
Dorsal view of a late presomite embryo (approx. 18 days) after removal of the amnion.

- Human heart starts to develop in middle of 3rd week of embryonic life.
- Till then, its needs are met by simple diffusion.
- Cardiac progenitor cells lie in the epiblast, immediately adjacent to cranial end of primitive streak.
- From there, they migrate through the streak into splanchnic layer of lateral plate mesoderm.
- To form horseshoe shaped cluster of cells – primary heart field (PHF)

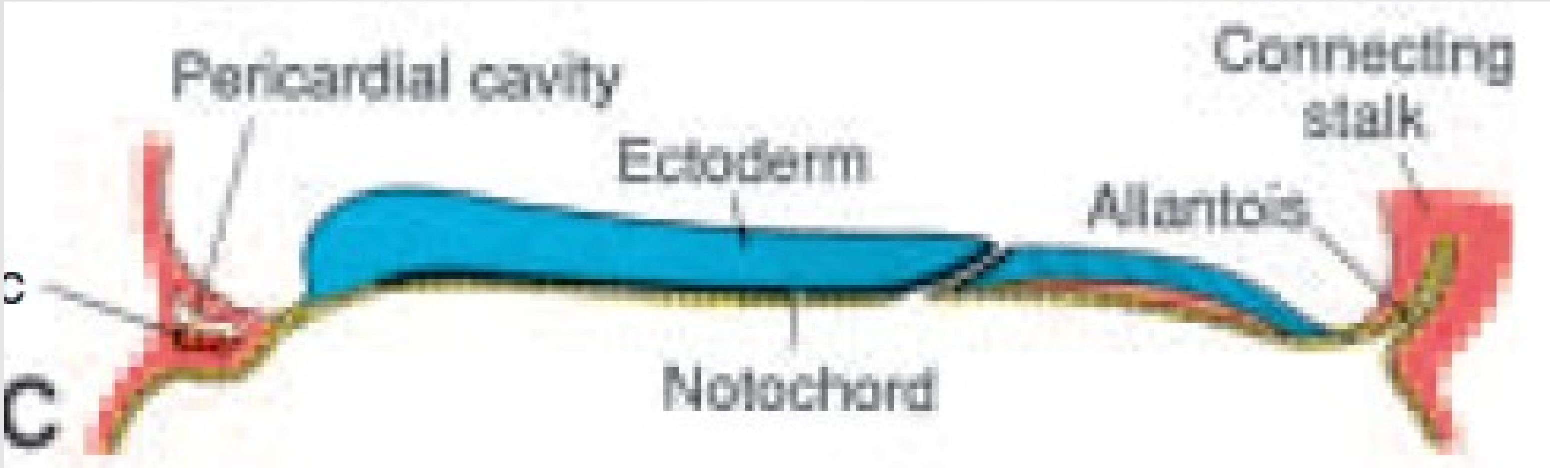


Transverse section showing position of the blood islands in splanchnic mesodermal layer.

- Cells in PHF are induced by the underlying pharyngeal endoderm to form cardiac myoblasts.
- With time, the islands unite and form a **horseshoe-shaped** endothelial-lined tube surrounded by myoblasts.
- This region is known as the **cardiogenic field.**
- Patterning of PHF occurs between 16-18 days, same time as that for the entire embryo.
- PHF is specified on both sides from lateral to medial to become atria, LV and most of RV.



Cephalocaudal section showing the position of the pericardial cavity and cardiogenic field.



- Intraembryonic cavity over cardiogenic field later develops into the **pericardial cavity**
- In addition to the cardiogenic region, other blood islands appear bilaterally, parallel and close to the midline of the embryonic shield.
- These islands form a pair of longitudinal vessels, the **dorsal aortae.**

Cardiac Precursor Cells

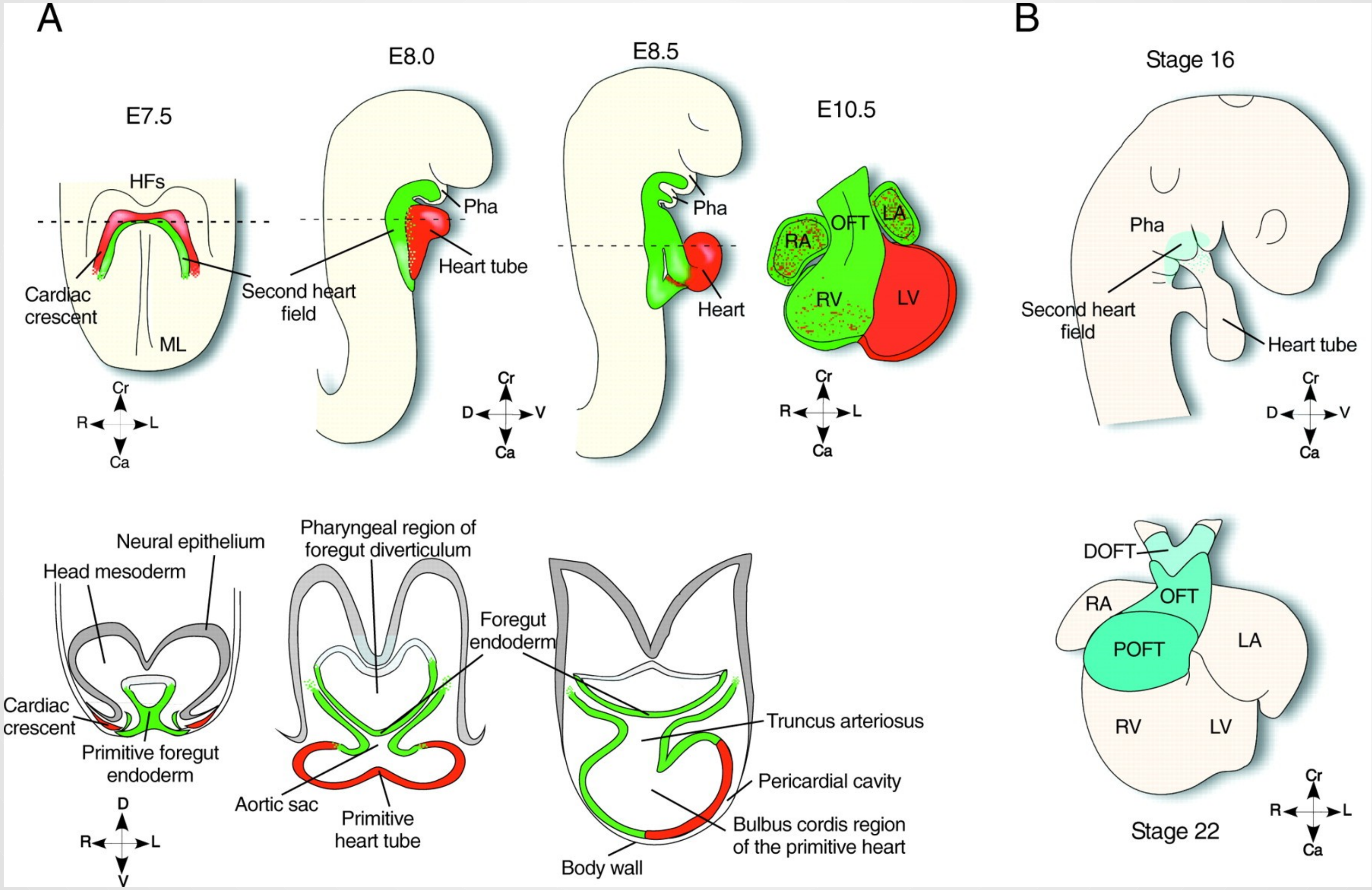
Derived from 4 sources :

1. Primary heart field (PHF)
2. Secondary heart field (SHF)
3. Cardiac neural crest cells (CNC)
4. Proepicardium

Concept of Heart Fields

- 2 distinct mesodermal heart fields that share a common origin appear to contribute cells to developing heart in a temporal and spatial specific manner.
- Using special techniques to mark progenitor cells these 2 heart fields have been characterised.
- The heart tube derived from PHF provides a scaffold that enables other cells to migrate and expand into cardiac chambers

Concept of Heart Fields



Secondary Heart Field

- Appears slightly late around days 20-21.
- Resides in splanchnic mesoderm, ventral to posterior pharynx.
- SHF forms part of RV and outflow tract (conus cordis and truncus arteriosus) .
- Exhibits laterality, such that those on right side contribute to left outflow tract and vice versa.

Cardiac Neural Crest Cells

- Neural crest cells, originate in the edges of the neural folds in the hindbrain region.
- Migrate through pharyngeal arches 3, 4, and 6 to the outflow region of the heart and contribute to endocardial cushion formation in both the conus cordis and truncus arteriosus.
- They also contribute to the formation of semilunar valves.
- Also contribute smooth muscle cells along the proximal segments of coronary arteries.
- Since neural crest cells also contribute to craniofacial development, it is not uncommon to see facial and cardiac abnormalities in the same individual.

Proepicardium

- Mesothelial cells on the surface of the septum transversum form the proepicardium near the sinus venous and migrate over the heart to form most of the epicardium.
- Responsible for formation of coronary arteries, including their endothelial lining and smooth muscle.

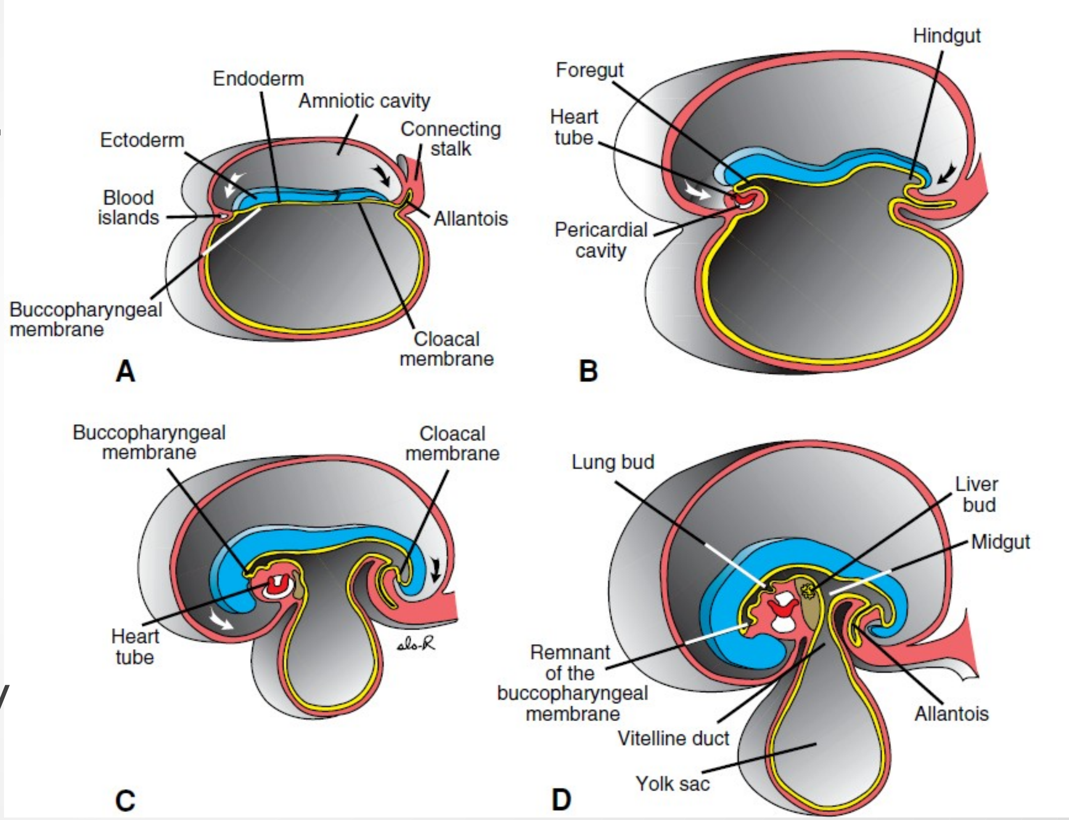
FORMATION AND POSITION OF THE HEART TUBE

Two processes responsible for positioning of the heart :

1. Folding of the embryo in a cephalocaudal direction
2. Folding of the embryo in a lateral direction

Cephalocaudal Folding

- Initially, cardiogenic area is anterior to the oropharyngeal membrane and the neural plate.
- Rapid cephalad growth of CNS extends it over the central cardiogenic area.
- Because of cephalic folding of the embryo, the oropharyngeal membrane is pulled forward.
- The heart and pericardial cavity move first to the cervical region and finally to the thorax

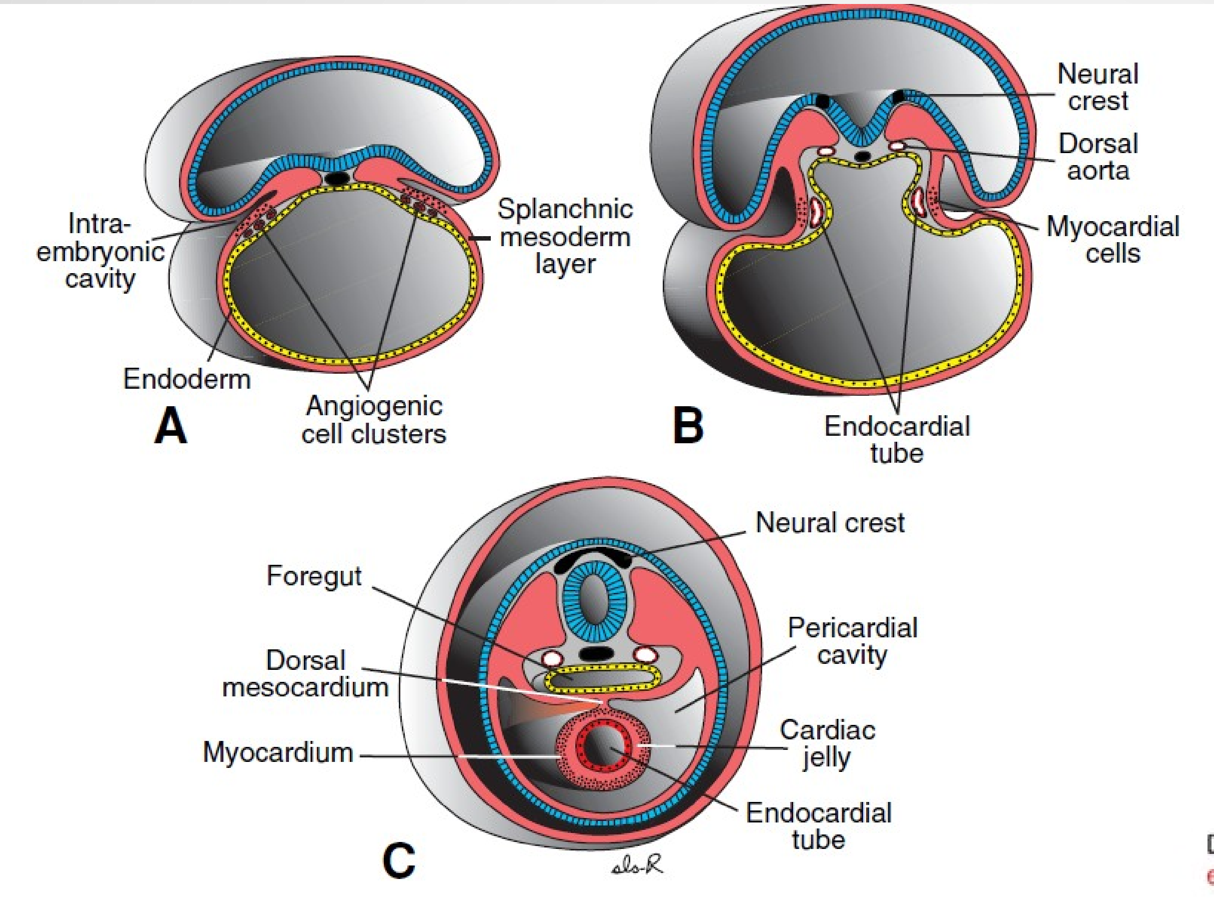


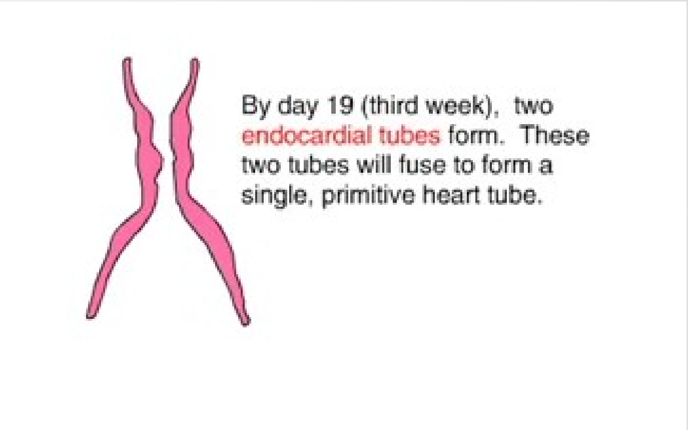
gures showing effects of the rapid growth of the brain on positioning of the hea
A. 18 days. B. 20 days. C. 21 days. D. 22 days

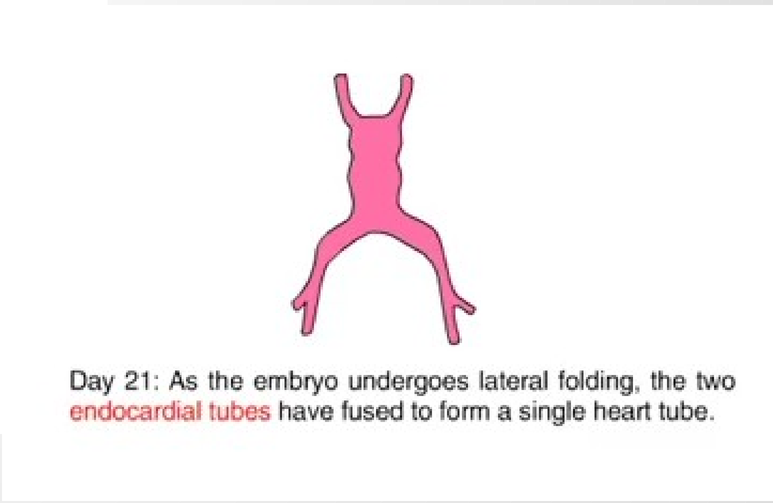
Lateral folding of the embryo

- Due to lateral folding, the pair of endothelial tubes merge except at their caudalmost ends.
- Simultaneously, the crescent part of the horseshoe-shaped area expands to form the future outflow tract and ventricular regions.
- Thus, the heart becomes a continuous expanded tube consisting of an inner endothelial lining and an outer myocardial layer.
- It receives venous drainage at its caudal pole and begins to pump blood out of the first aortic arch into the dorsal aorta at its cranial pole.

ateral folding of the embry







Development of layers of myocardium

- During these events, the myocardium thickens and secretes a thick layer of extracellular matrix, rich in hyaluronic acid, that separates it from the endothelium called **cardiac jelly**.

- In addition, mesothelial cells on the surface of the septum transversum form the **proepicardium** near the sinus venous and migrate over the heart to form most of the epicardium.

- The remainder of the epicardium is derived from mesothelial cells originating in the outflow tract region.

- Thus, the heart tube consists of three layers:

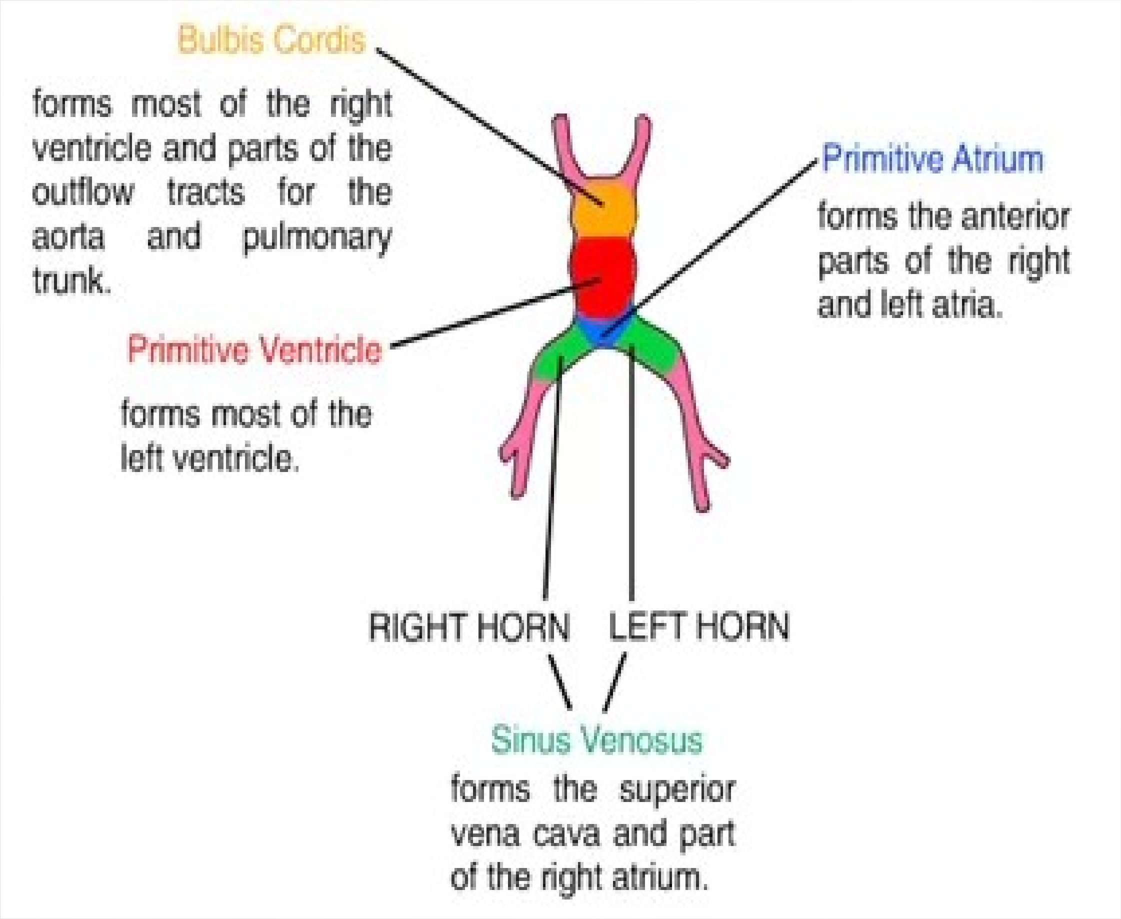
1. Endocardium – forming the internal lining of the tube;
2. Myocardium – forming the muscular wall;
3. Epicardium or visceral pericardium – covering the outside of the tube.

- This epicardium is responsible for formation of the coronary arteries, including their endothelial lining and smooth muscle.

Development of Pericardium

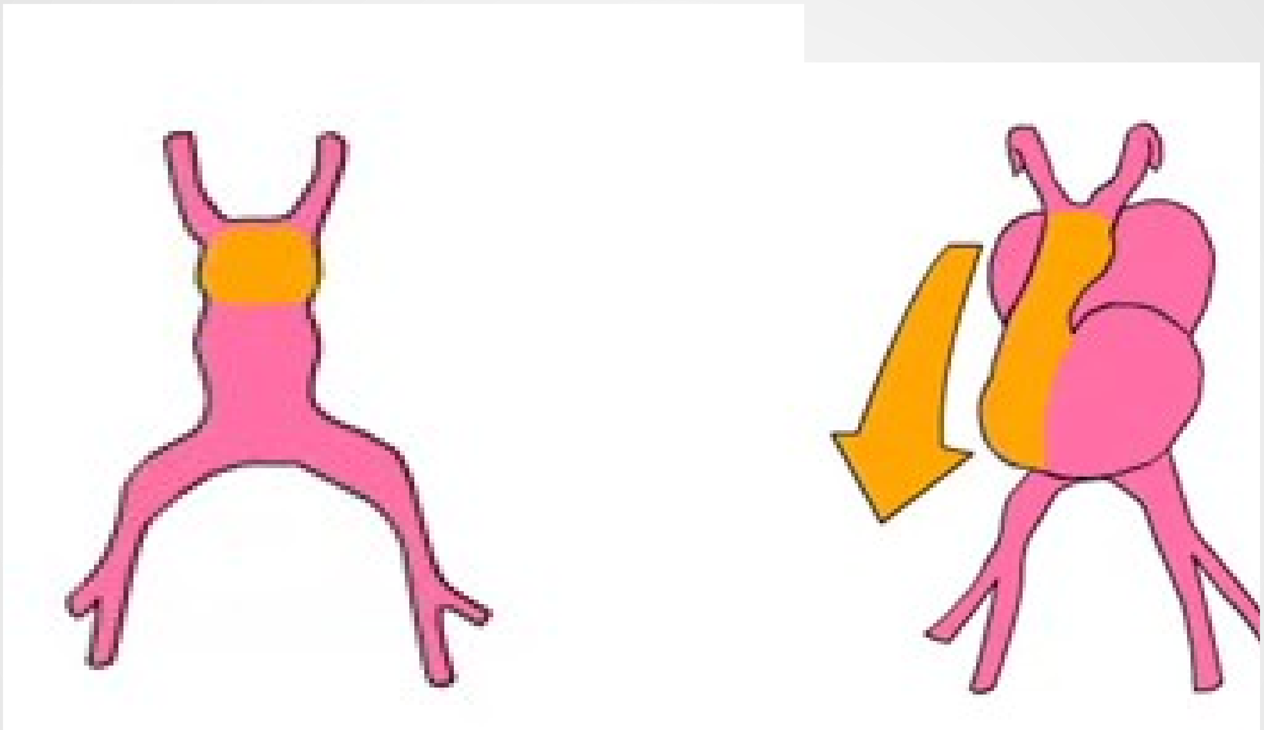
- The developing heart tube bulges more and more into the pericardial cavity.
- Initially, the tube remains attached to the dorsal side of pericardial cavity by the dorsal mesocardium.
- No ventral mesocardium is ever formed.
- With further development, the dorsal mesocardium disappears, creating the transverse pericardial sinus, which connects both sides of pericardial cavity.
- The heart is now suspended in the cavity by blood vessels at its cranial and caudal poles

Formation of the Cardiac Loop



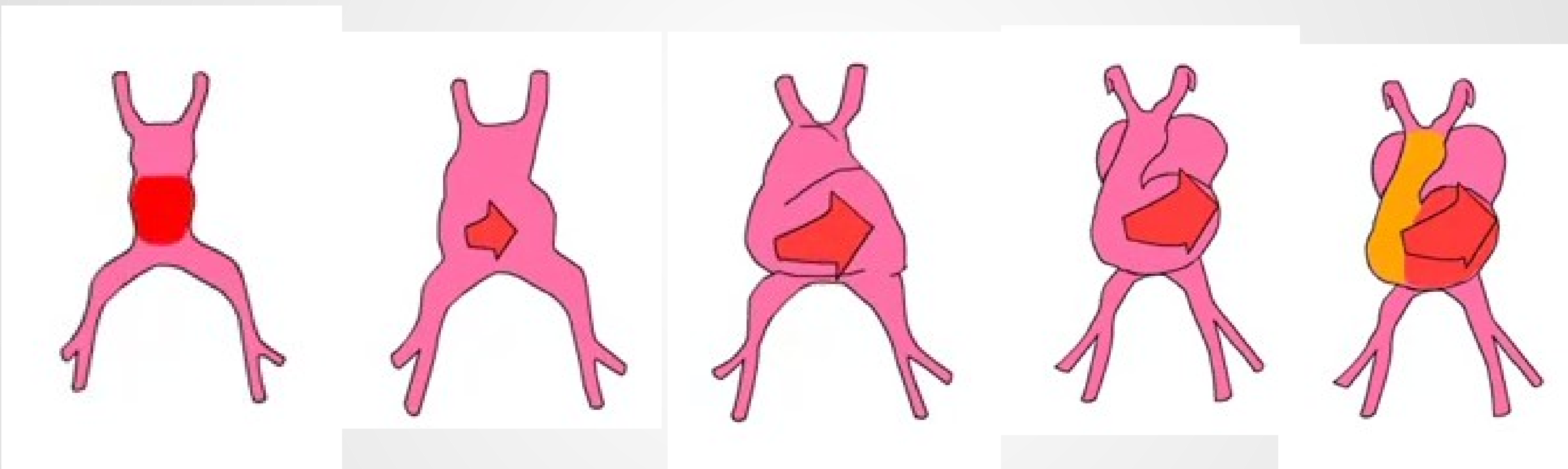
- The heart tube starts to bend on day 23.
- The cephalic portion of the tube bends ventrally, caudally, and to the right .
- The atrial (caudal) portion shifts dorsocranially and to the left.
- This bending creates the cardiac loop which is complete by day 28

Bulbus Cordis



the bulbis cordis moves inferiorly, anteriorly and to the embryo's right

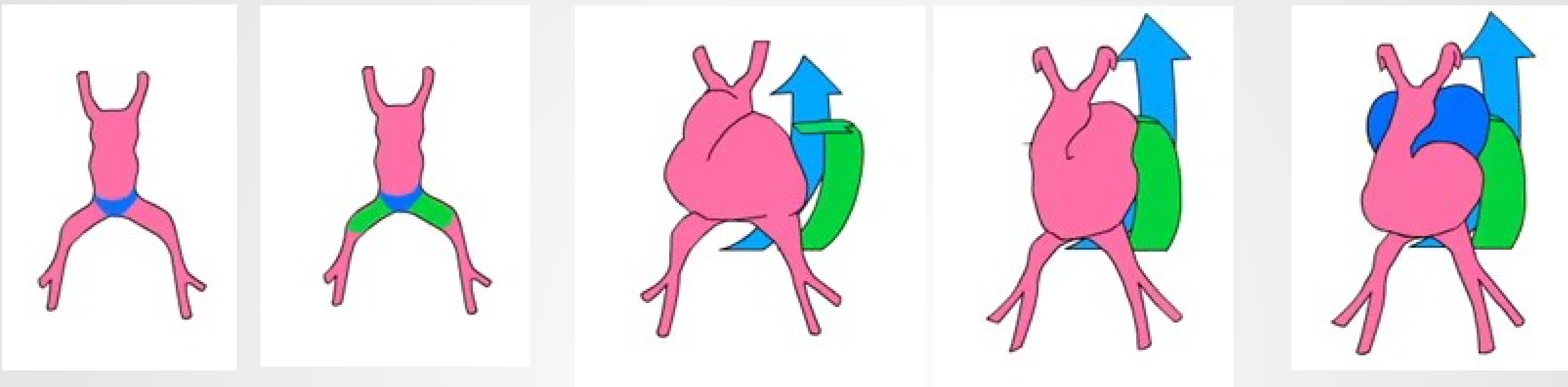
Primitive Ventricle

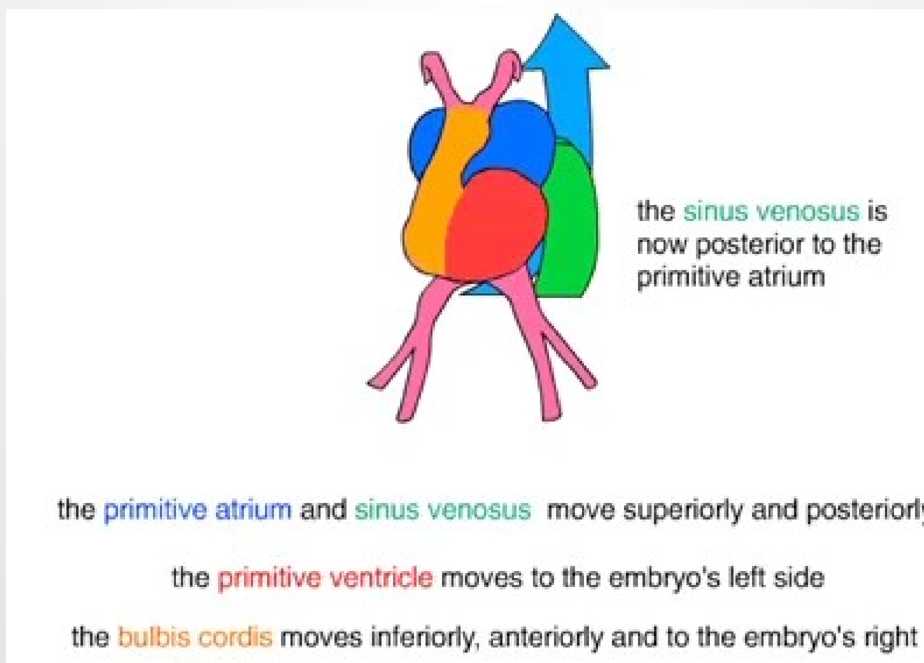


the primitive ventricle moves to the embryo's left side

the bulbis cordis moves inferiorly, anteriorly and to the embryo's right

The Primitive Atrium and Sinus Venosus





- The **bulbus cordis** develops 3 divisions :
  - Proximal part – forms the trabeculated part of RV.
  - Midportion (**conus cordis**) – forms the outflow tracts of both ventricles.
  - Distal part (**truncus arteriosus**) – forms the roots and proximal portion of the aorta and pulmonary artery.
- The junction between the primitive ventricle and the bulbus cordis (**bulboventricular sulcus**) remains narrow. It is called the **primary interventricular foramen .**
- Evidence suggests that **homeobox genes** regulate organization of these segments

- The smooth walled heart tube begins to form primitive trabeculae proximal and distal to the primary interventricular foramen.

- The bulbus temporarily remains smooth walled.

- The primitive ventricle, which is now trabeculated, is called the **primitive LV**.

- Likewise, the trabeculated proximal third of the bulbus cordis may be called the **primitive RV**.

- The **atrial portion**, initially a paired structure outside the pericardial cavity, forms a common atrium and is incorporated into the pericardial cavity.
- The **AV junction** remains narrow and forms the **AV canal**, which connects the common atrium and the early embryonic ventricle
- The **conotruncal portion**, initially on the right side, shifts gradually to a more medial position due to formation of 2 transverse dilations of the atrium, bulging on each side of the bulbus cordis .

abnormal cardiac looping

Dextrocardia :

- Heart lies on the right side of the thorax instead of the left.
- Because the heart loops to the left instead of the right.
- May coincide with situs inversus

Molecular Regulation of Cardiac Development

of Cardiac Development

- Anterior (cranial) endoderm induces a heart-forming region by inducing the transcription factor **NKX2.5**.

- The signals require secretion of **BMPs 2 and 4** secreted by the endoderm and lateral plate mesoderm.

- Concomitantly, the activity of **WNT proteins (3a and 8)** secreted by the neural tube, must be blocked because they normally inhibit heart development.

- Inhibitors (crescent and cerberus) of the WNT proteins are produced by endoderm cells immediately adjacent to heart-forming mesoderm.

- The combination of **BMP activity and WNT inhibition** by crescent and cerberus causes expression of NKX2.5

# of Cardiac Development

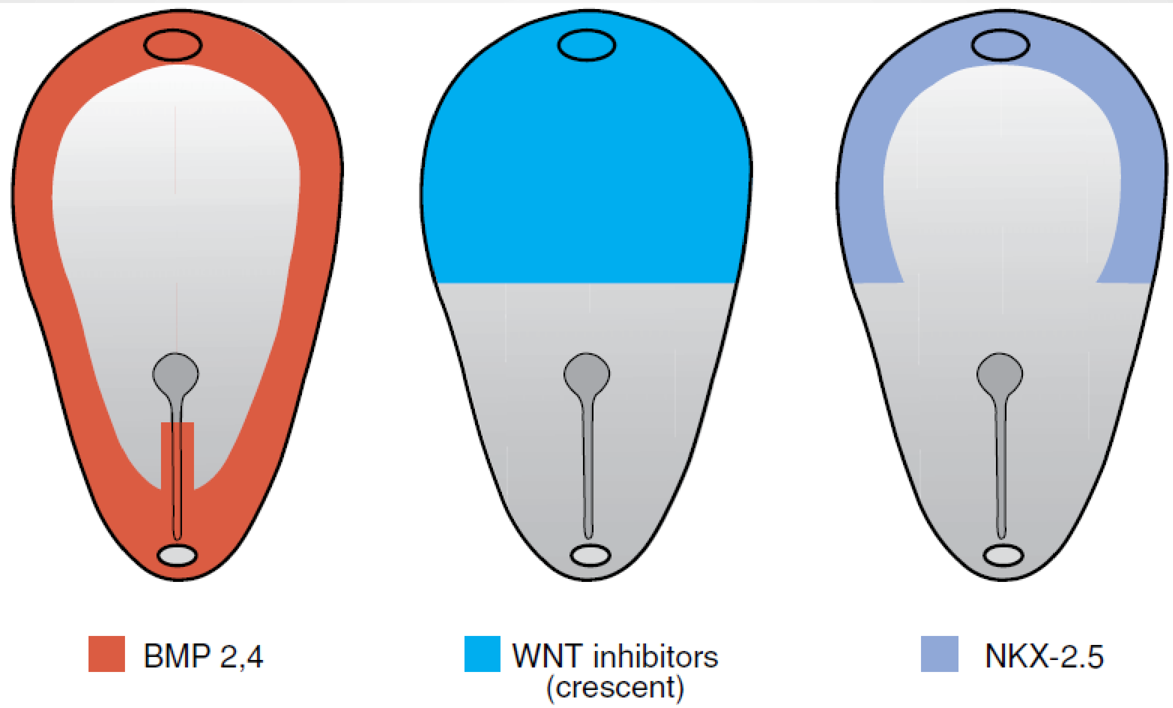


Figure 11.9 Heart induction. BMPs secreted in the posterior portion of the primitive streak and periphery of the embryo, in combination with inhibition of *WNT* expression by *crescent* in the anterior half of the embryo, induce expression of *NKX2.5* in the heart forming region of the lateral plate mesoderm (splanchnic layer). *NKX2.5* is then responsible for heart induction.

- BMP upregulates expression of FGF8 that is important for the expression of cardiac-specific proteins.

- Once the cardiac tube is formed, the **venous portion** is specified by **retinoic acid (RA)** produced by mesoderm adjacent to the presumptive sinus venosus and atria.

- Following this initial exposure to RA, these structures express the gene for **retinaldehyde dehydrogenase**, which allows them to make their own RA and commits them to becoming caudal cardiac structures.

- Lower concentrations of RA in more anterior cardiac regions (ventricles and outflow tract) contribute to specification of these structures.

- This explains why the compound can produce a variety of cardiac defects.

- **TBX5** is another transcription factor that contains a DNA binding motif known as the T-box, plays an important role in **septation**.

- **Cardiac looping** is dependent in part upon the laterality-inducing genes **nodal** and **lefty2**.

- These genes induce expression of the transcription factor **PITX2**.

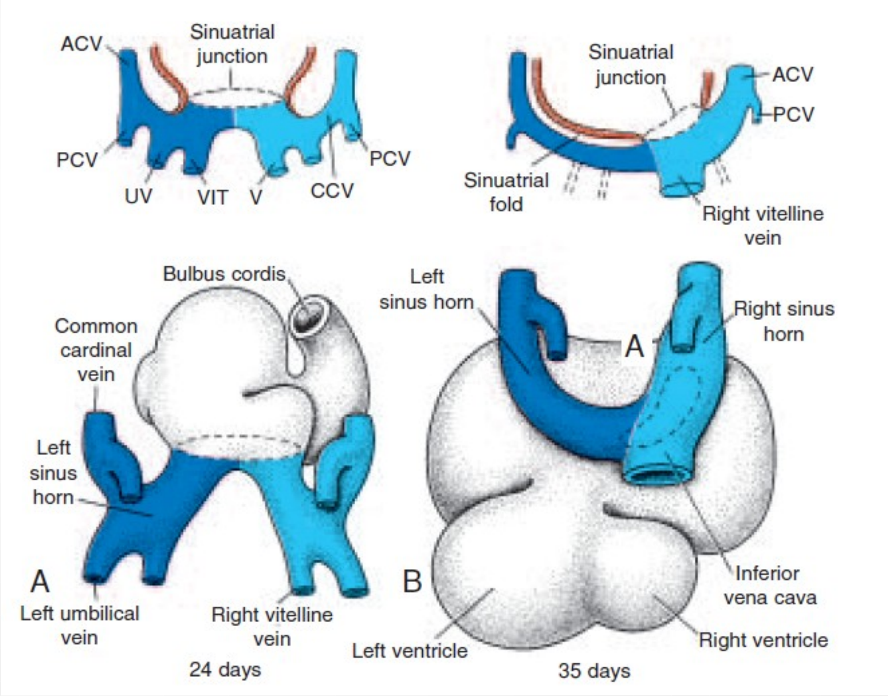
- **PITX2** may play a role in the deposition and function of extracellular matrix molecules during looping.

- **NKX2.5** upregulates expression of **HAND1** and **HAND2** , which are expressed in the primitive heart tube and later become restricted to the future **left and right ventricles**.

Development of the Sinus Venosus

Development of the Sinus Venosus

- In mid **4th week**, the sinus venosus receives venous blood from **the right and left sinus horns**.
- Each horn receives blood from 3 important veins:
  1. **vitelline or omphalomesenteric vein,**
  2. **umbilical vein,**
  3. **common cardinal vein**.
- Entrance of the sinus shifts to the right primarily caused by **left-to-right shunts** of blood occuring in the venous system.
- The right horn, now the only communication between the original SV and the atrium, is

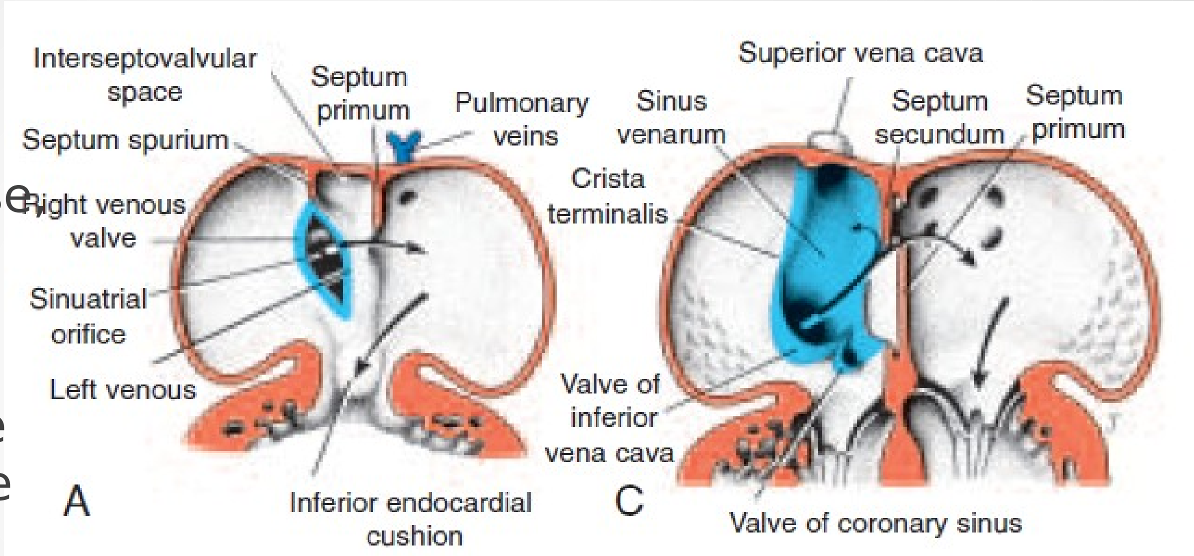


Development of Venous Valves

The **sinuatrial orifice**, is flanked on each side by a valvular fold, the **right and left venous valves**.

Dorsocranially, the valves fuse, forming a ridge known as the **septum spurium**.

The left venous valve and the septum spurium fuse with the developing atrial septum.



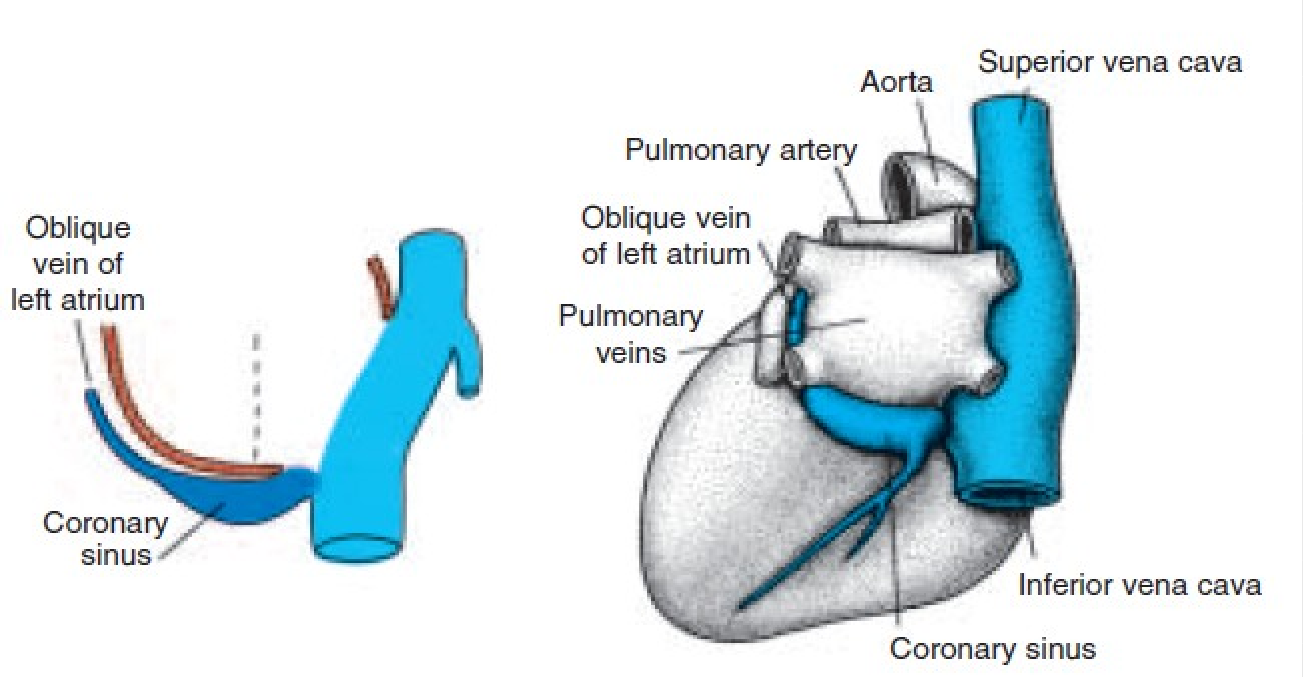
The **superior portion** of the right venous valve disappears entirely.

The **inferior portion** develops into two parts:

(1) **valve of the inferior vena cava**
(2) **valve of the coronary sinus**.

- The **crista terminalis** forms the dividing line between the original trabeculated part of the RA and the smooth-walled part,from the right sinus horn

Development of the Sinus Venosus



When the left common cardinal vein is obliterated at **10 weeks**, all that remains of the left sinus horn is the **oblique vein of the LA and coronary sinus**

Formation of the Cardiac Septae

Formation of the Cardiac Septae

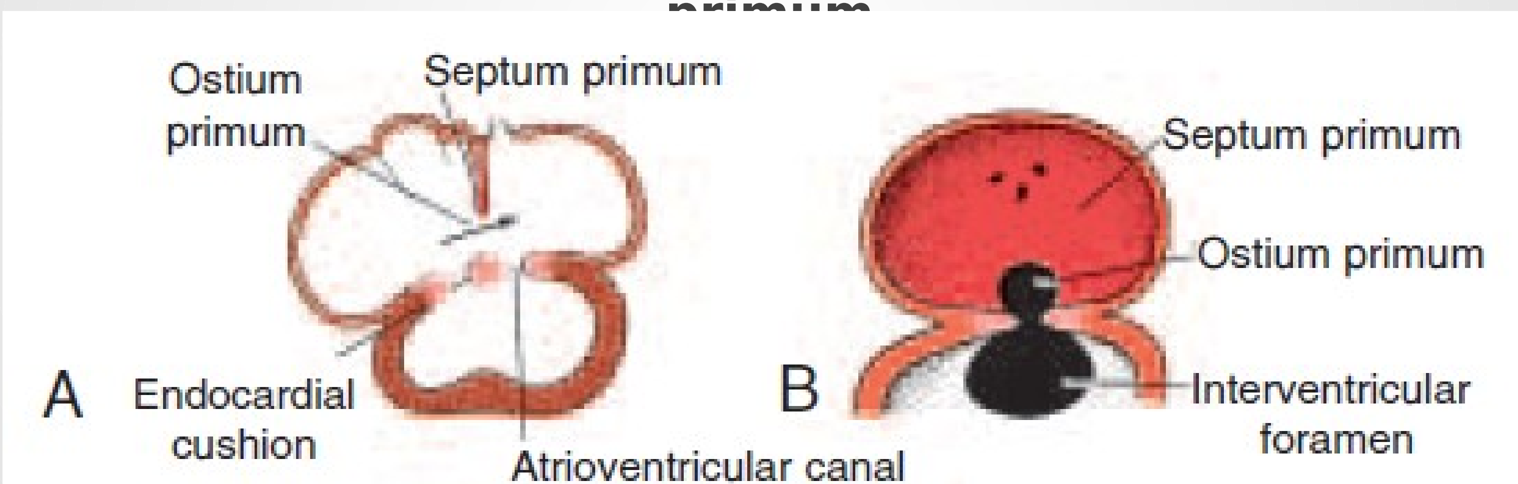
- The major septae are formed between the **27 and 37th days** of development

- It is a simultanuous process if the following areas

1. Septum formation in the common atrium
2. Septum formation in the atrioventricular canal
3. Septum formation in the truncus arteriosus and conus cordis
4. Septum formation in the ventricles

Septum formation in the Common Atria

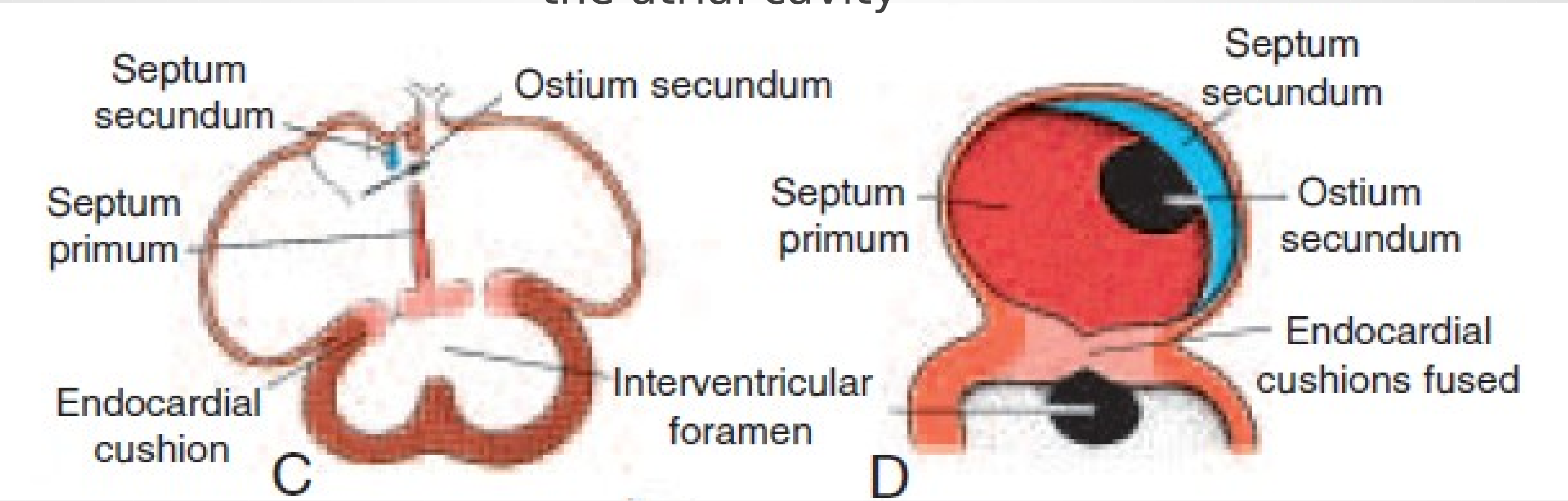
At the end of the **4th week**, a sickle-shaped crest grows from the roof of the common atrium into the lumen. This crest is the first portion of the **septum primum**



A. 30 days .
B. Same stage as **A,** viewed from the right.

Septum formation of the Common Atria

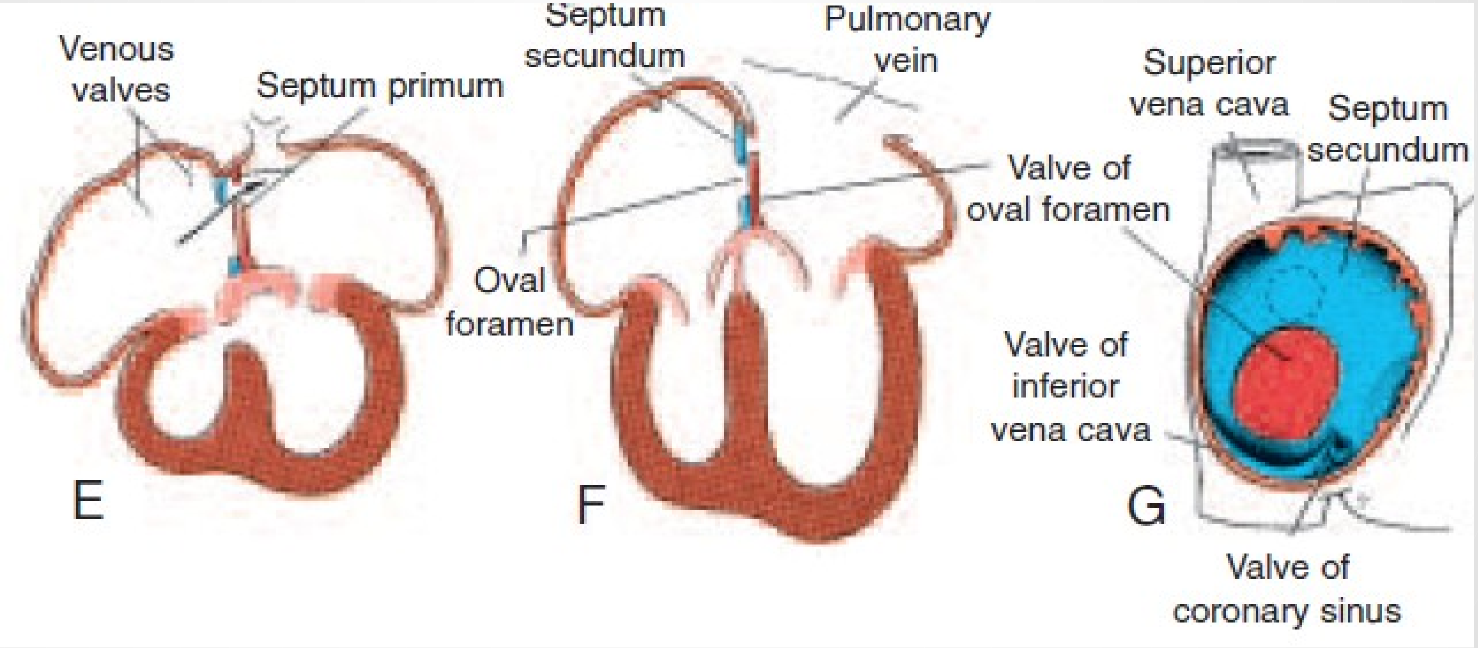
When the lumen of the right atrium expands as a result of incorporation of
the sinus horn, a new crescent-shaped fold appears. This new fold, the **septum secundum** never forms a complete partion in the atrial cavity



C. 33 days.
D. Same stage as **C,** viewed from the right

Septum formation of the common atria

When the upper part of the septum primum gradually disappears, the
remaining part becomes the **valve of the oval foramen.**



E. 37 days; **F.** Newborn.
G. The atrial septum from the right; same stage as **F.**

Further differentiation of the Atria

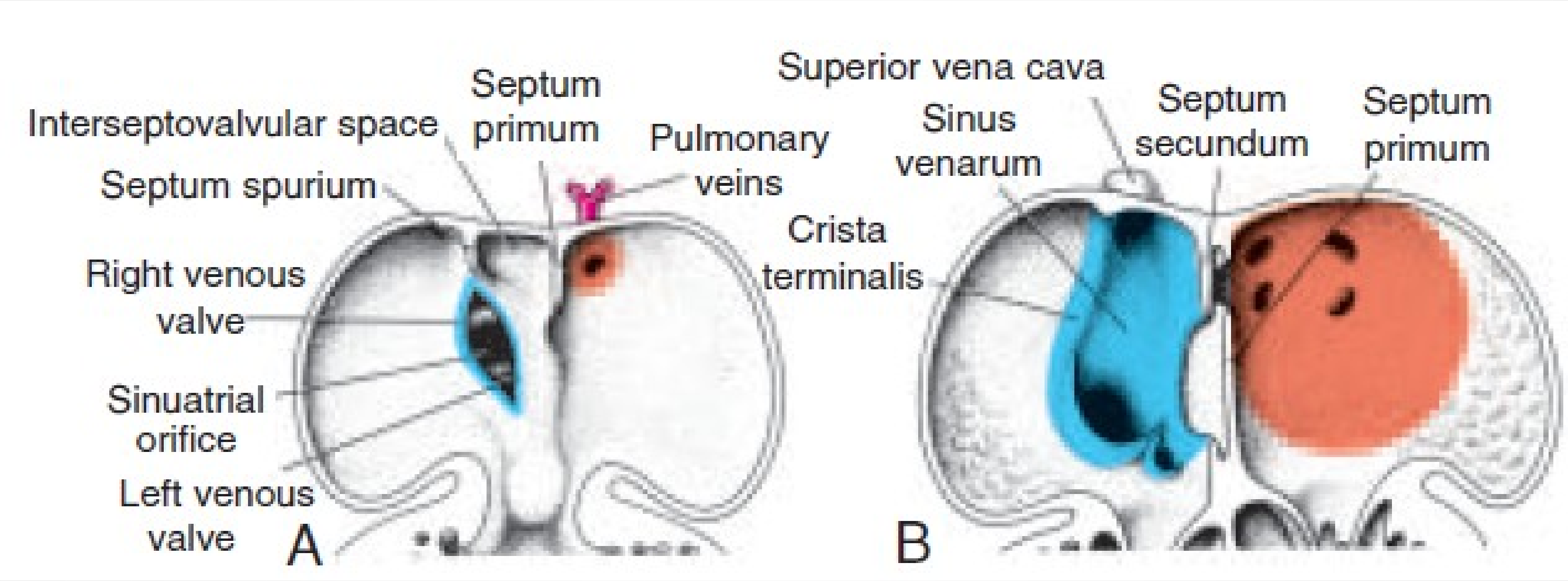
- **Primitive RA** enlarges by incorporation of the right sinus horn.

- From **Primitive LA**, a **single embryonic pulmonary vein** develops as an outgrowth of the posterior left atrial wall, just to the left of the septum primum.

- This vein gains connection with veins of the developing lung buds.

- During further development, the **4 Pulmonary Veins** are incorporated, forming the large smooth walled part of the adult LA.

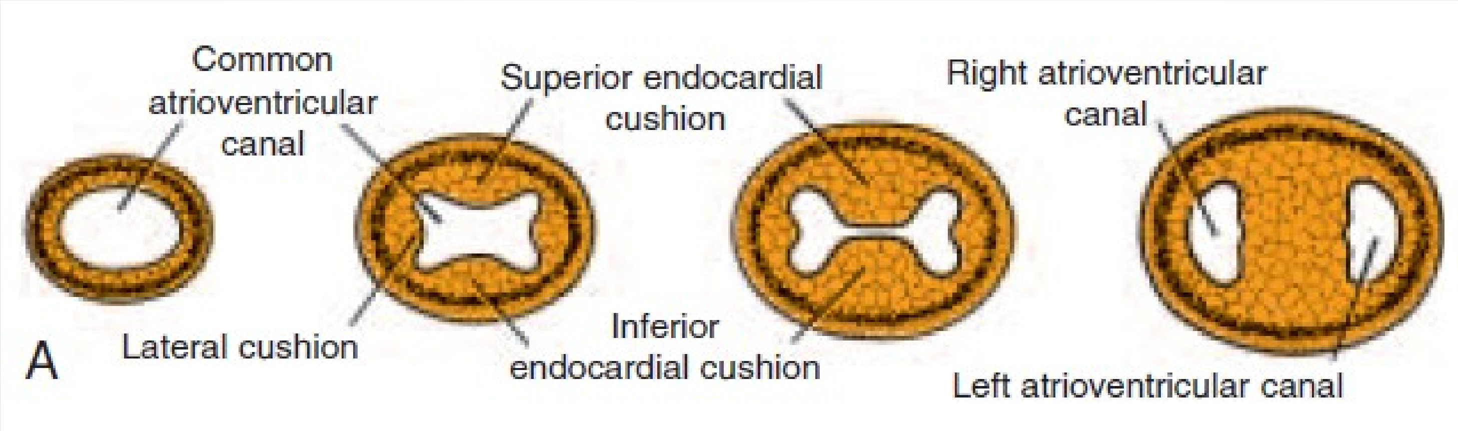
Further differentiation of the Atria



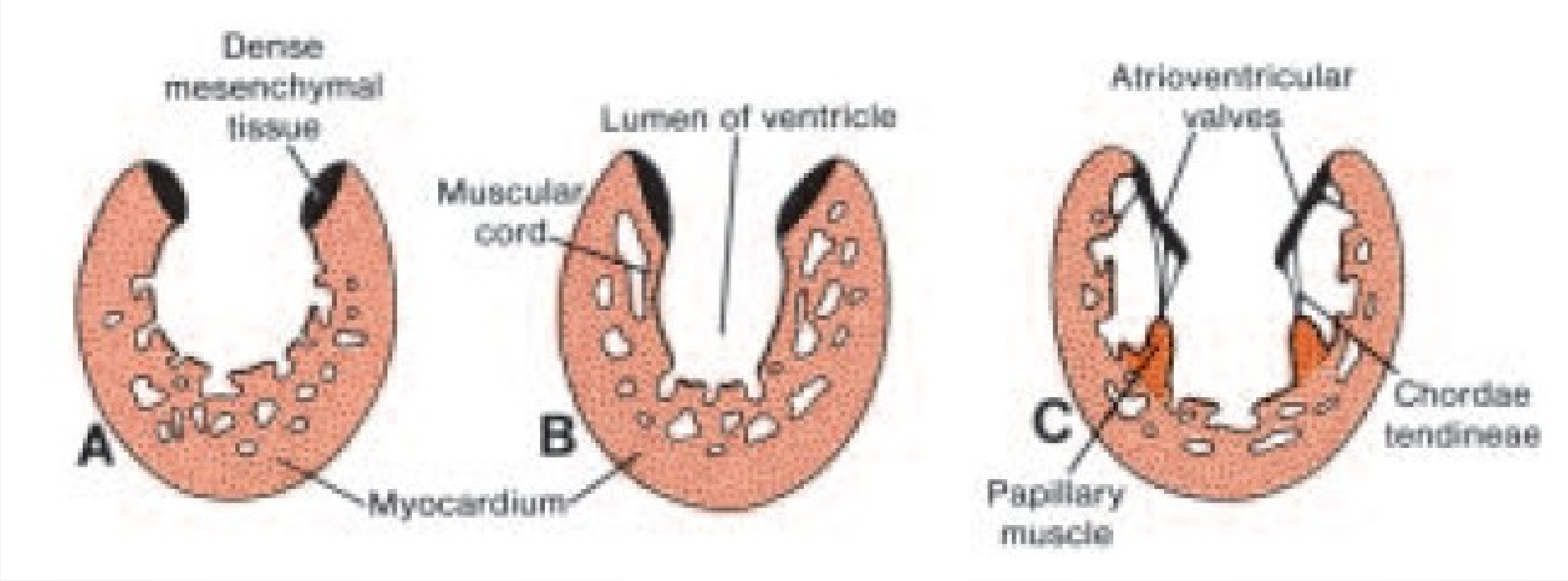
Both the wall of the right sinus horn (*blue*) and the pulmonary veins (*red*) are incorporated into the heart to form the smooth-walled parts of the atria.

the Atrioventricular Canal

- At the end of the **4th week**, two mesenchymal cushions, the **atrioventricular endocardial cushions,** appear at the **superior** and **inferior** borders of the atrioventricular canal, two additional lateral cushions appear at the **left and right** borders.
- At the end of the **5th week** there is complete fusion of the superior and inferior cushions with complete division of the canal into left and right orifices.



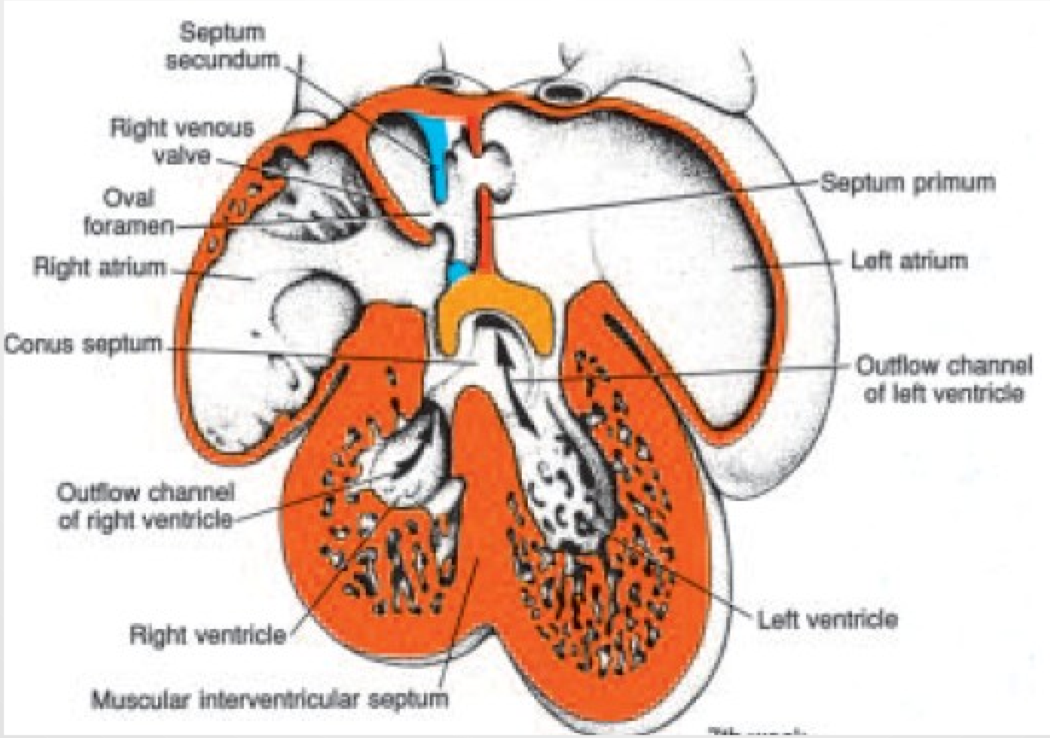
Atrioventricular Valves



- After the endocardial cushions fuse, each AV orifice is surrounded by local proliferations of mesenchymal tissue.
- Bloodstream hollows and thins out tissue on the ventricular surface of these proliferations, forming valves that remain attached to the ventricular wall by muscular cords.
- Finally, muscular tissue in the cords degenerates and is replaced by dense connective tissue.

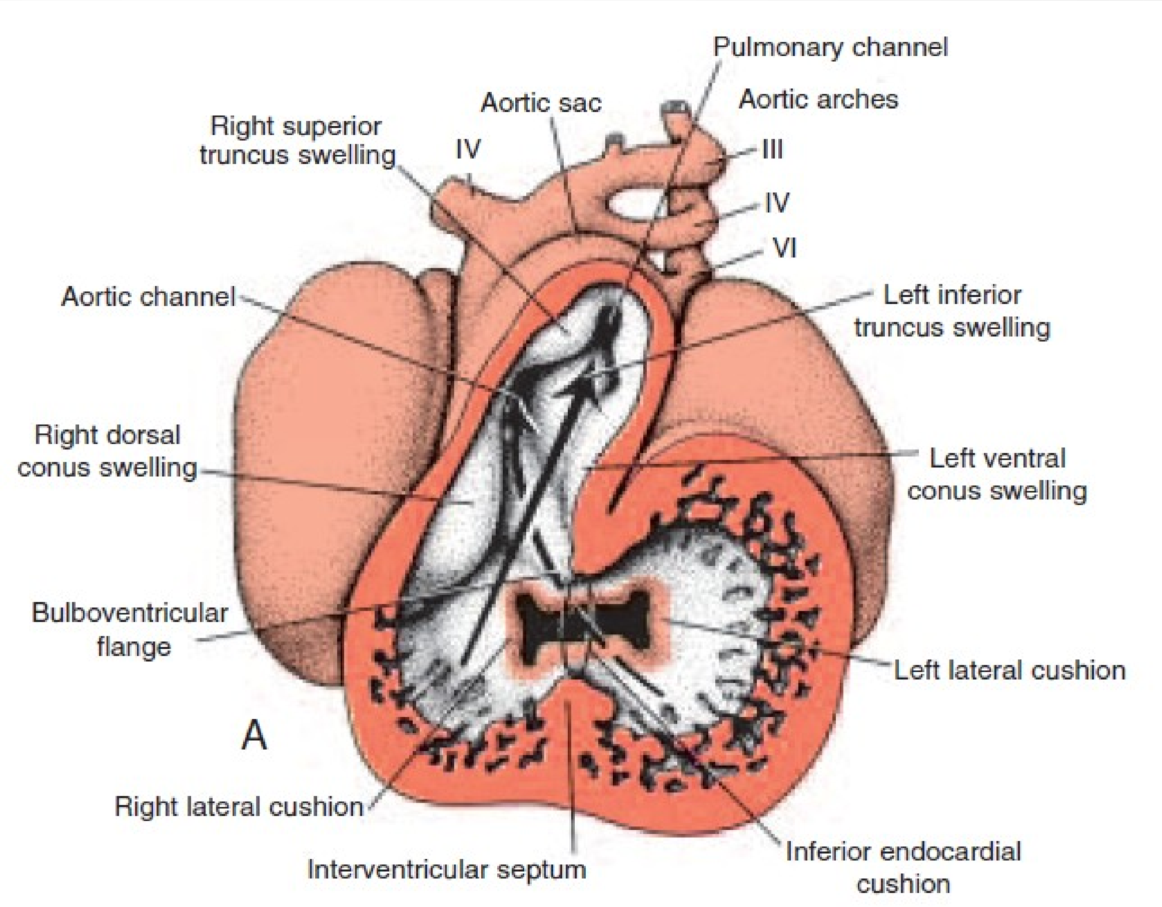
Septum formation of the Ventricles

- **End of the 4th week** the two primitive ventricles start to expand.
- The medial walls of the expanding ventricles become apposed and gradually merge, forming the **muscular interventricular septum**



Septum formation of the Truncus Arteriosus and Conus Cordis

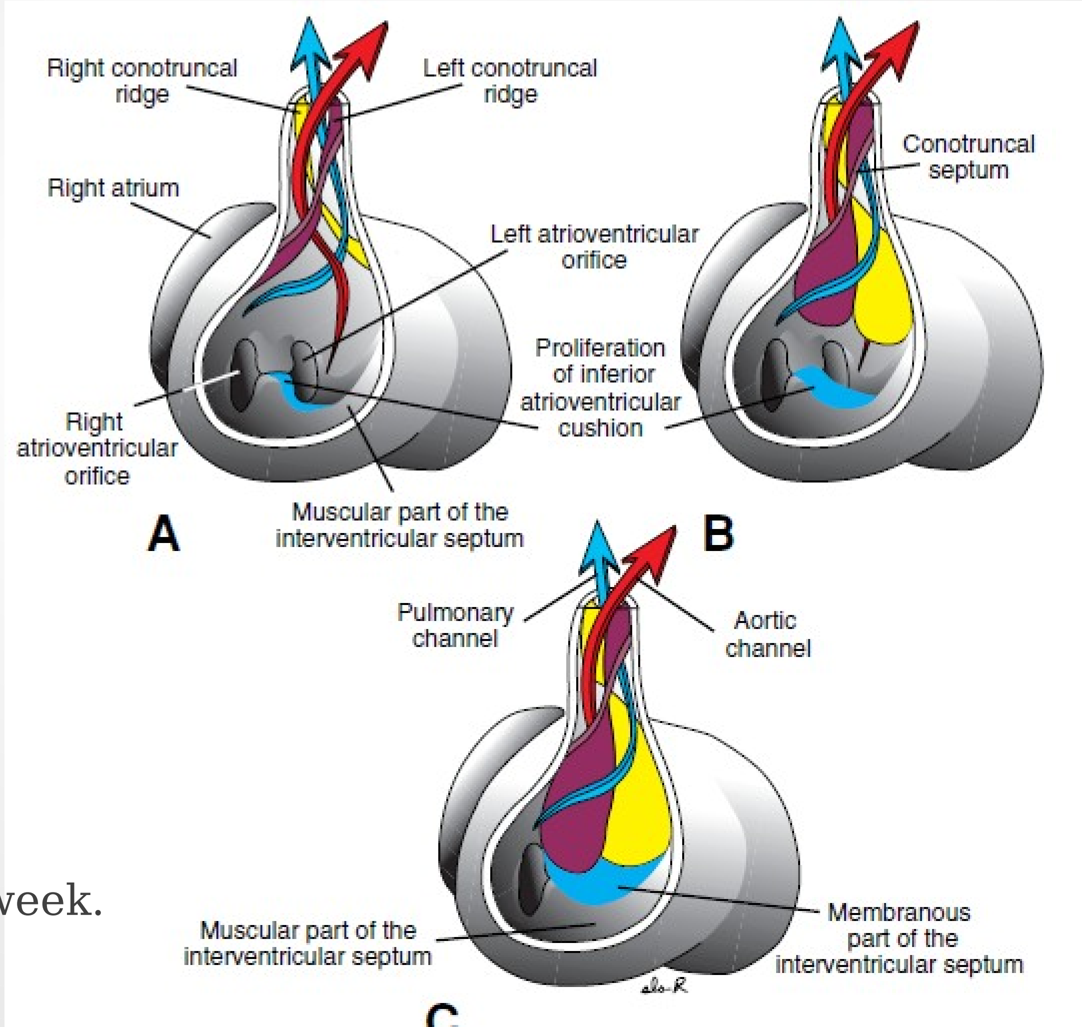
5th week, pairs of opposing ridges appear in the truncus and conus cordis



Interventricular Septum

- Combined Proliferations of the **right and left conus cushions**, along with the **inferior endocardial cushion**

- Close the interventricular foramen and form the **membranous portion of the interventricular septum**.



A. 6 weeks.

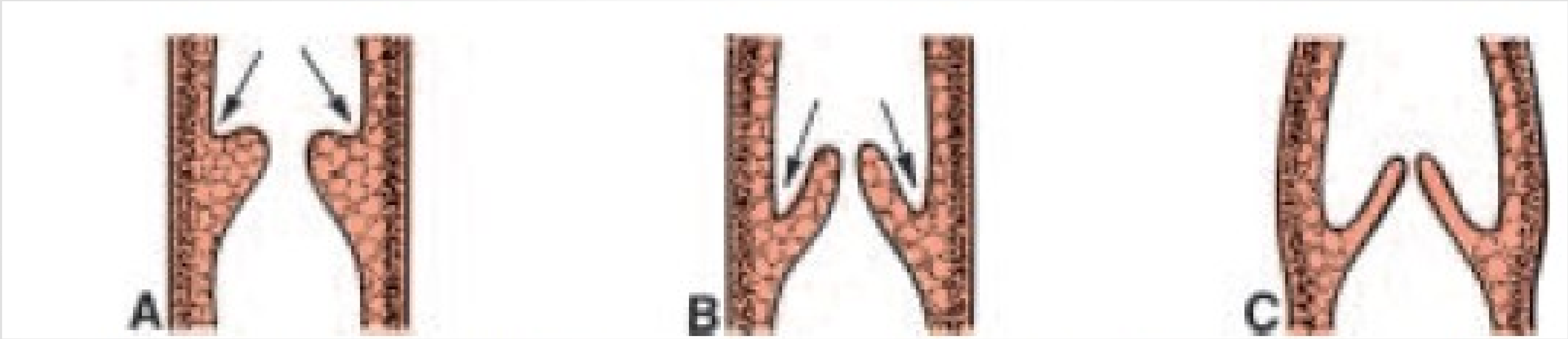
B. Beginning of the 7th week.

- C. End of the 7th week.

Semilunar Valves

- When partitioning of the truncus is almost complete, primordia of the semilunar valves become visible as **pair of small tubercles** found on the **main truncus swellings.**
- **One of each pair** is assigned to **the pulmonary and aortic channels,** respectively
- A **third tubercle** appears in both channels opposite the fused truncus swellings.
- Gradually the tubercles hollow out at their upper surface, forming the **semilunar valves**.
- Recent evidence shows that **neural crest cells** contribute to formation of these valves.

Longitudinal section through the semilunar valves



6 weeks 7 weeks 9 week

Clinical correlates ASD related defects

1. ASD
2. Endocardial cushion defects (AV canal defects)
3. Tricuspid atresia

Clinical correlates ASD related defects

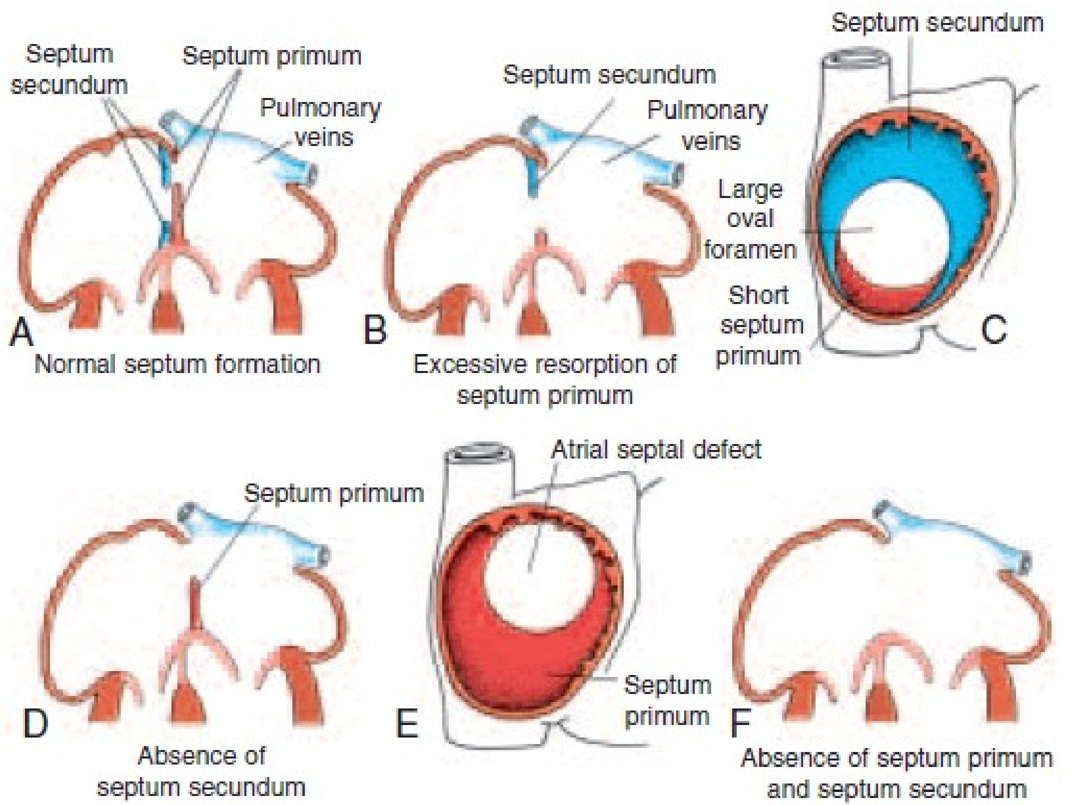


Figure 11.19 A. Normal atrial septum formation. **B** and **C.** Ostium secundum defect caused by excessive resorption of the septum primum. **D** and **E.** Similar defect caused by failure of development of the septum secundum. **F.** Common atrium, or cor triloculare biventriculare, resulting from complete failure of the septum primum and septum secundum to form.

Persistent common AV canal

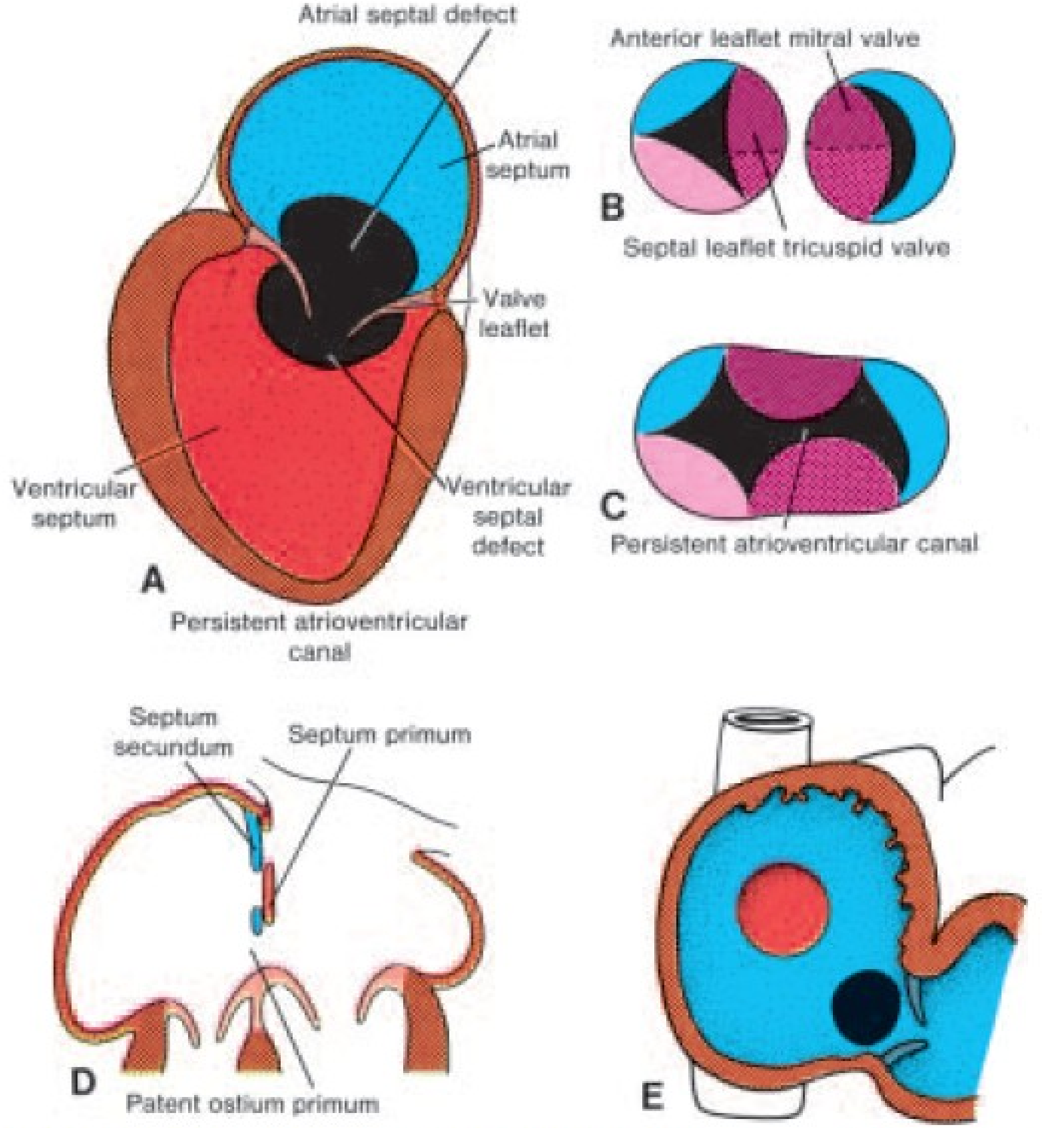


Figure 11.20 A. Persistent common atrioventricular canal. This abnormality is always accompanied by a septum defect in the atrial as well as in the ventricular portion of the cardiac partitions. **B.** Valves in the atrioventricular orifices under normal conditions. **C.** Split valves in a persistent atrioventricular canal. **D** and **E.** Ostium primum defect caused by incomplete fusion of the atrioventricular endocardial cushions.

Tricuspid Atresia

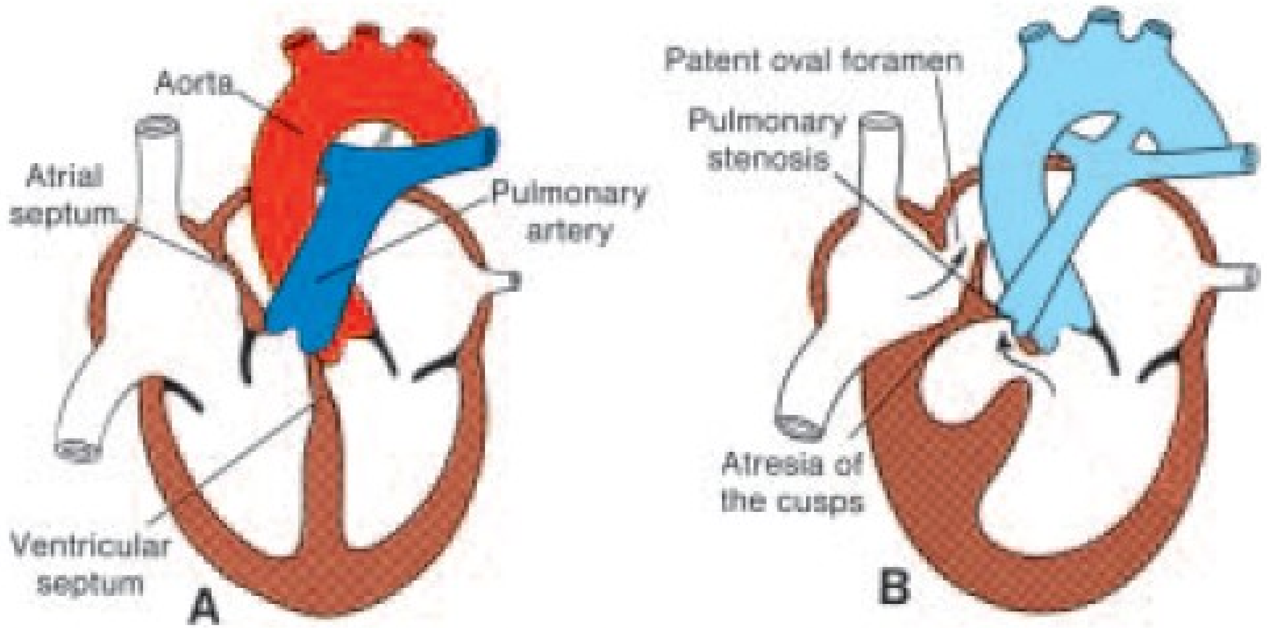


Figure 11.21 A. Normal heart. **B.** Tricuspid atresia. Note the small right ventricle and the large left ventricle.

Clinical correlates VSD related defects

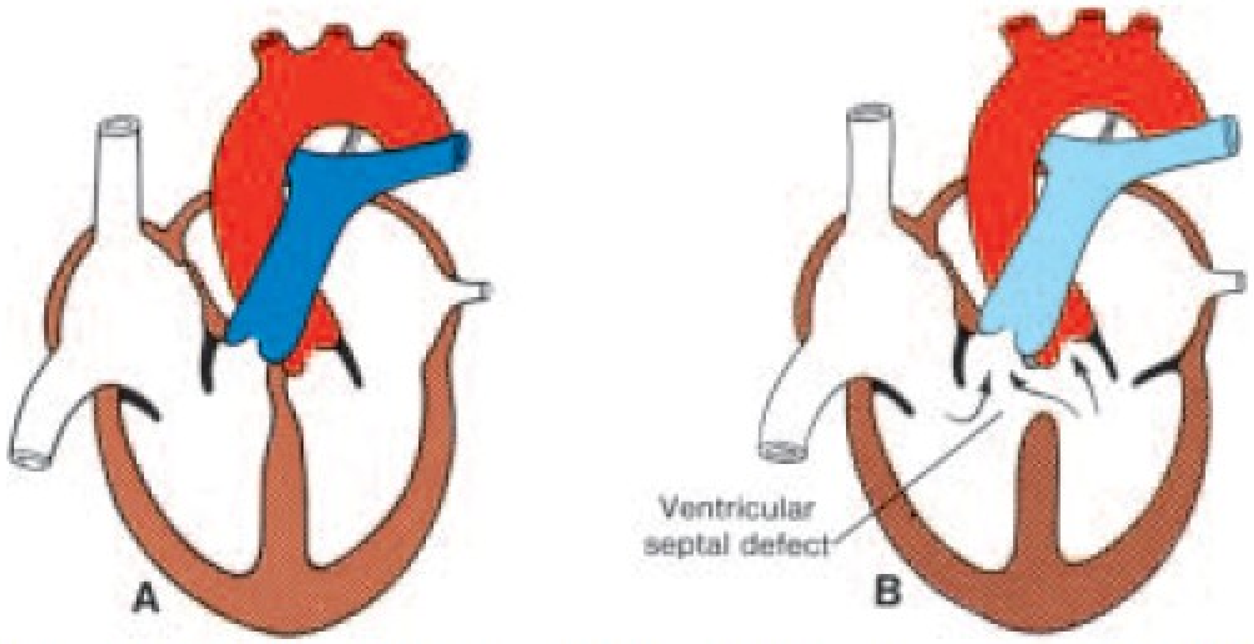
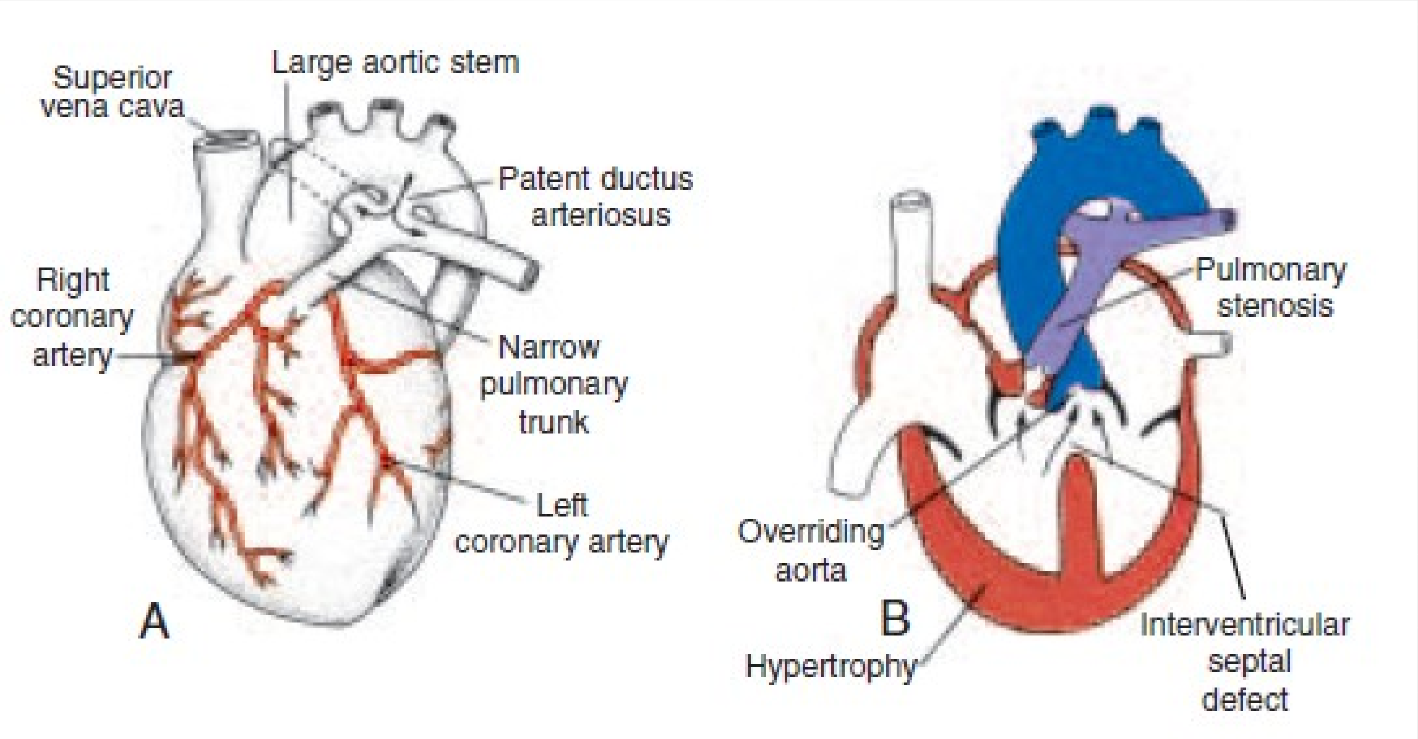


Figure 11.28 A. Normal heart. **B.** Isolated defect in the membranous portion of the interventricular septum. Blood from the left ventricle flows to the right through the interventricular foramen (*arrows*).

Tetralogy of Fallot



Persistent truncus arteriosus

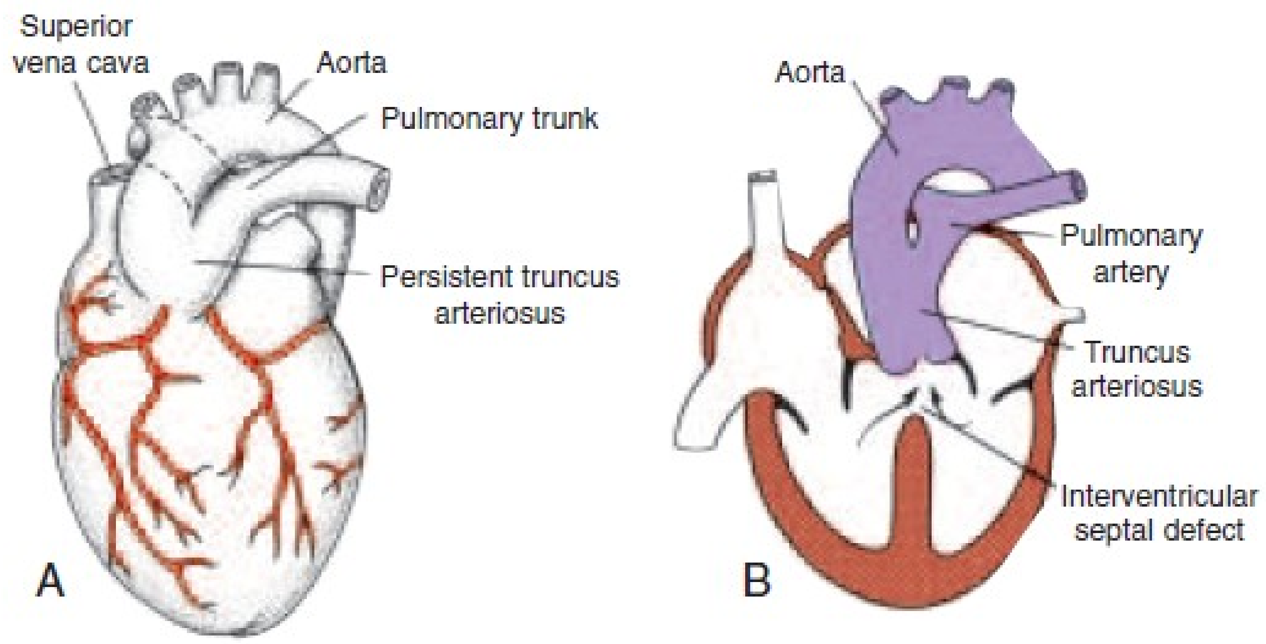


Figure 11.30 Persistent truncus arteriosus. The pulmonary artery originates from a common truncus (**A**). The septum in the truncus and conus has failed to form (**B**). This abnormality is always accompanied by an interventricular septal defect.

vessels
Pulmonar valvular atresia

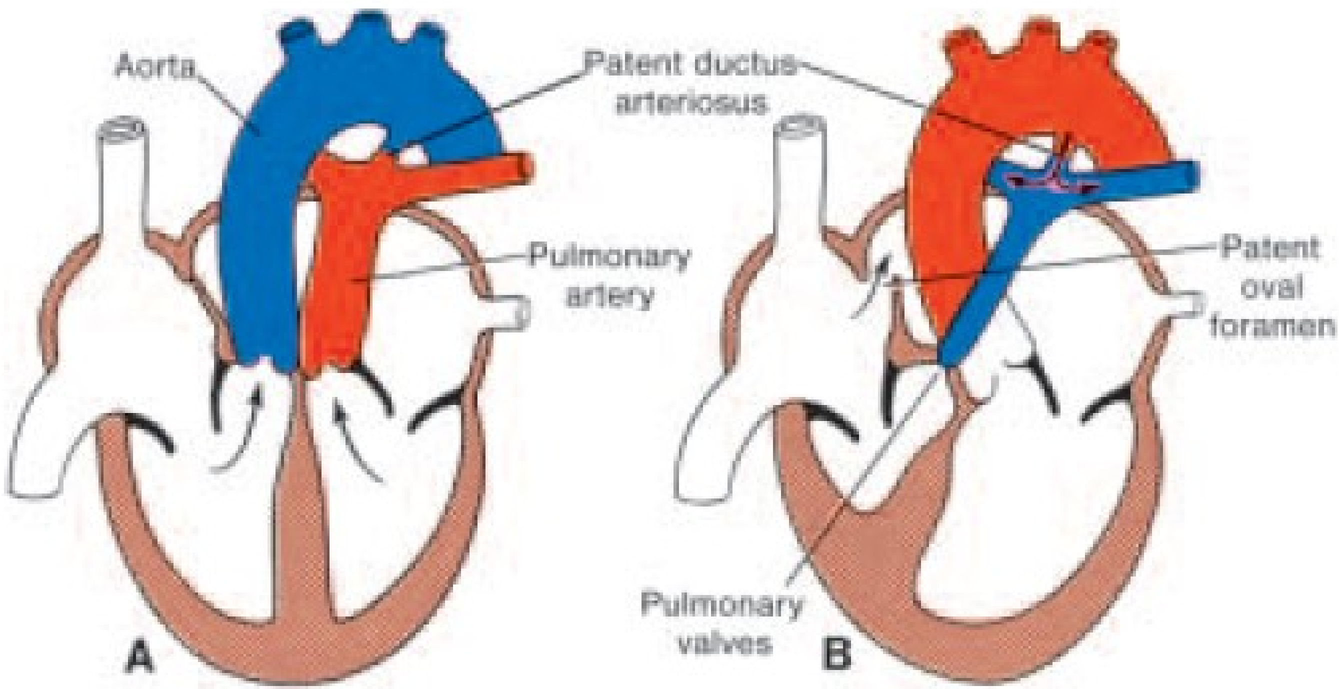


Figure 11.31 A. Transposition of the great vessels. **B.** Pulmonary valvular atresia with a normal aortic root. The only access route to the lungs is by way of a patent ductus arteriosus.

Conducting System of the Heart

Sinu Atrial Node :

- Initially the pacemaker for the heart lies in the caudal part of the left cardiac tube.
- Later the sinus venosus assumes this function.
- As the sinus is incorporated into the right atrium, pacemaker tissue lies near the opening of the superior vena cava. Thus, the sinuatrial node is formed.

Atrio Ventricular Node and Bundle of His :

- The atrioventricular node and bundle (bundle of His) are derived from two sources:
  1. cells in the left wall of the sinus venosus
  2. cells from the AV canal.

- Once the sinus venosus is incorporated into the RA, these cells lie in their final position at the base of the interatrial septum.

Vascular Development

- Arterial system
- Venous system

- Blood vessel development occurs by two mechanisms:

  1. **vasculogenesis** – vessels arise by coalescence of angioblasts (Eg: major vessels like **Dorsal Aorta** and **Cardinal Veins**)

  2. **Angiogenesis** – vessels sprout from existing vessels. (remainder of vascular system)

- The entire system is patterned by **vascular endothelial growth factor (VEGF)** and other growth factors

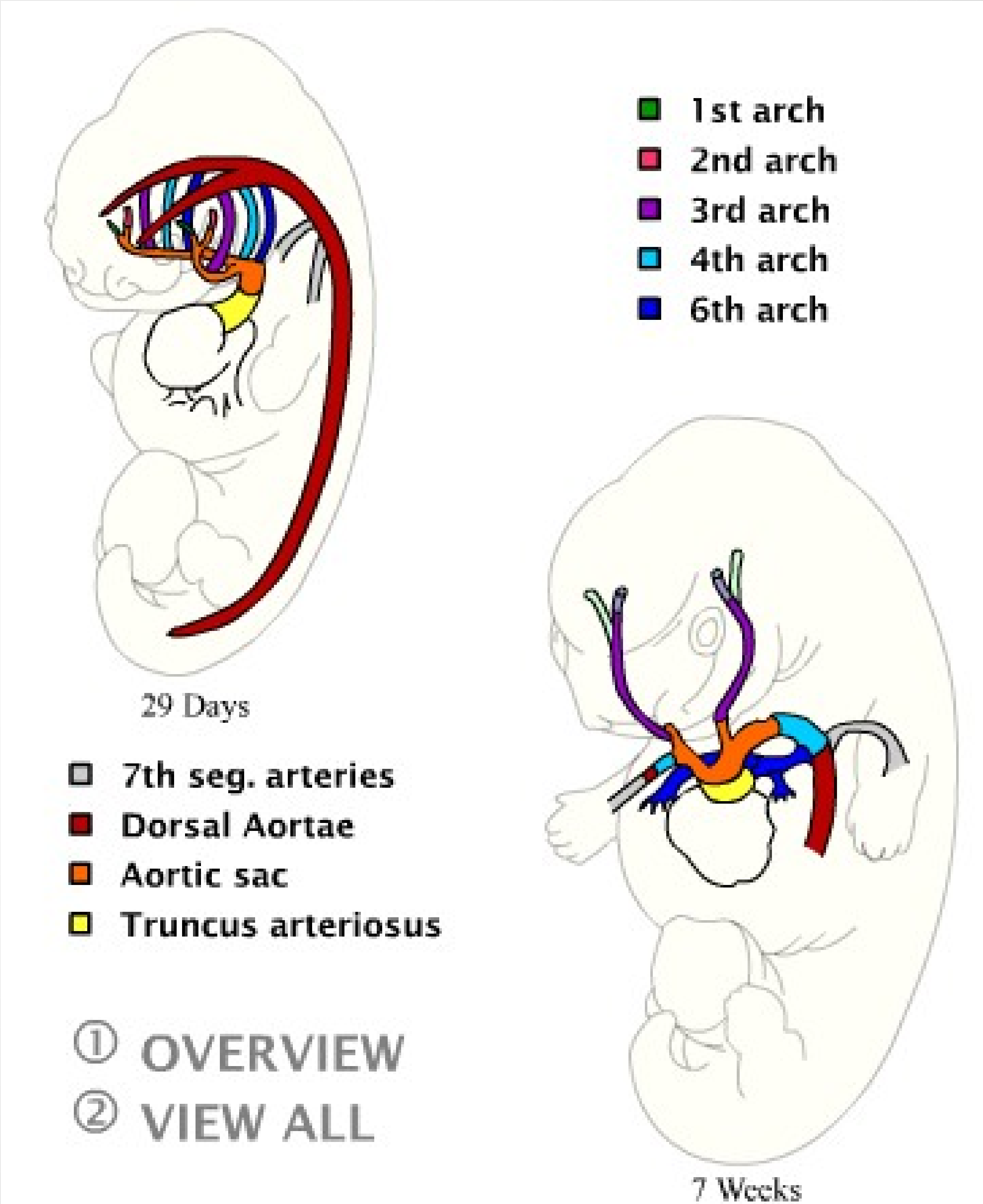
Arterial System

- Aortic Arches
- Vitelline Arteries
- Umbilical arteries

Aortic Arches

- During **4th and 5th week**
- Arise from the **aortic sac (truncus arteriosus)** and embedded in the mesenchyme of pharyngeal arches
- Each arch receives its **own cranial nerve** and its **own artery**.
- Terminate in the **left and right dorsal aorta**
- These arches and vessels appear in a **cranial to caudal sequence** and
  not all simultanously
- The **aortic sac** also forms **left and right horns** which give rise
  to the **Brachiocephalic Artery** and **Proximal Arch**
respectively

Aortic arches



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Development of Aortic Arches

- By **day 27**, most of the **1st aortic arch** has disappeared, only a small portion persists to form the **maxillary artery**.
- By **day 29**, the **2nd aortic arch** also disappears, remanants are the **hyoid and stapedial arteries**.
- The **3rd, 4th, and 6th arches** are large.
- The **5th aortic arch** either never forms or forms incompletely and then regresses.
- Once the conotruncal region divides, the 6th arches now become continuous with the pulmonary trunk.

- **The 3rd Aortic Arch** :
  - Forms the **Common Carotid Artery (CCA)** and the first part of the **Internal Carotid Artery (ICA).**
  - The remainder of the ICA is formed by the cranial portion of the dorsal aorta.
  - The **External Carotid Artery (ECA)** is a sprout of the 3rd aortic arch.

- **The 4th Aortic Arch :**
  - Persists on both sides.
  - Ultimate fate is different on the right and left sides.
  - **On the left**, forms **part of the arch of the aorta**, between the left CCA and the left subclavian arteries.
  - **On the right**, forms the most proximal segment of the **right subclavian artery**, the distal part of which is formed by a portion of the right dorsal aorta and the 7th intersegmental artery

- **The 6th Aortic Arch :**
  - Also known as the **Pulmonary Arch.**
  - On both sides, the **proximal part** becomes the proximal segment of the **Right and Left Pulmonary Artery**.
  - **On the right**, the **distal portion** of this arch loses its connection with the dorsal aorta and **disappears**.
  - **On the left**, the **distal part** persists during intrauterine life as the **Ductus Arteriosus**

- **Other Changes During Alterations In The Aortic Arch System:**

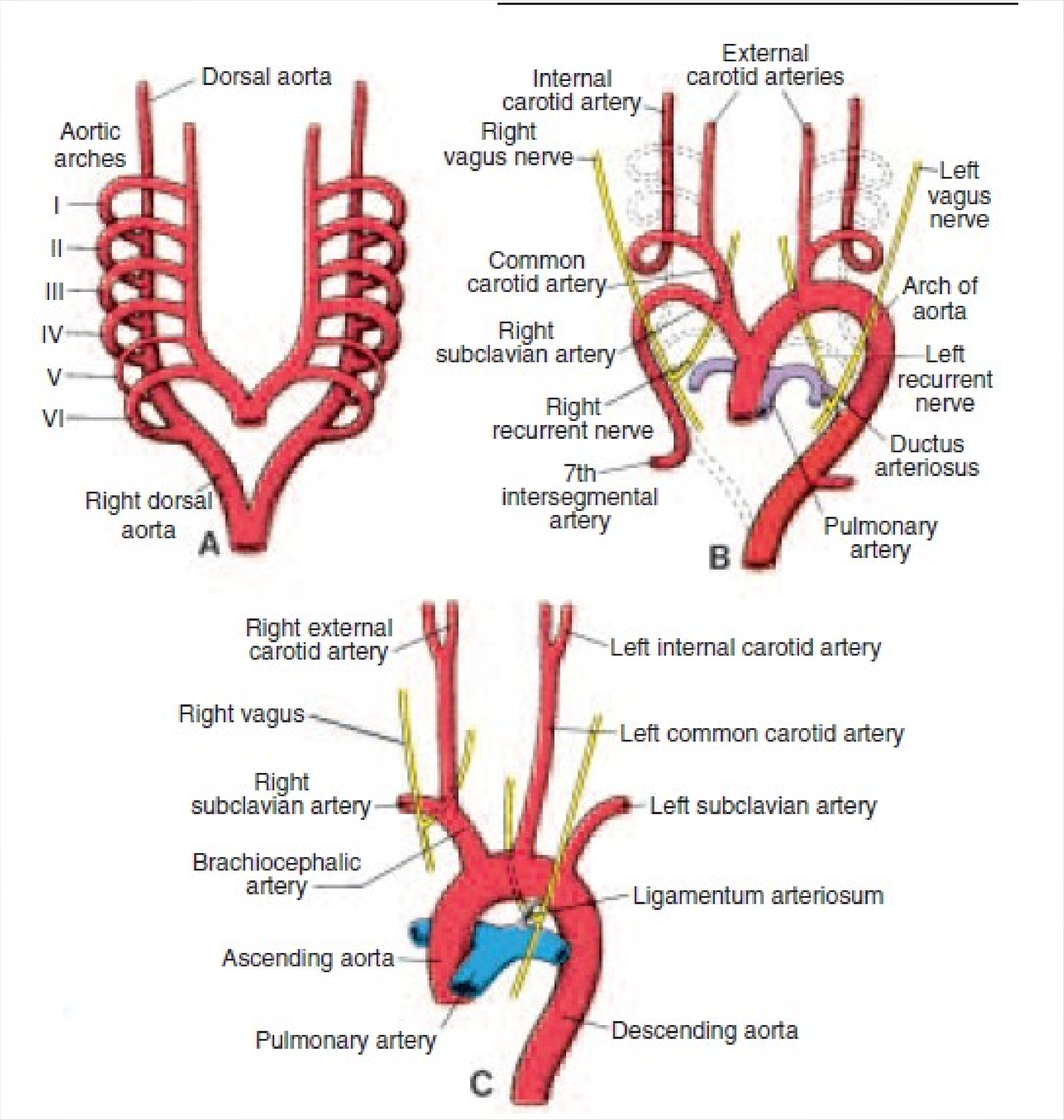
1. The dorsal aorta between the entrance of the third and fourth arches, known as the **Carotid Duct,** is obliterated ;

2. The **right dorsal aorta disappears** between the origin of the 7th intersegmental artery and its junction with left dorsal aorta;

3. **Cephalic folding** pushes heart into the thoracic cavity. Hence, the **carotid and brachiocephalic arteries elongate** considerably.

4. The course of the **Recurrent Laryngeal Nerves**

e Of Recurrent Laryngeal Nerves On Both Si



Aortic arches

Aortic Arch Vessels Development (Day 29 to Week 7)

Vessels	Left	Right
1st arch	Regress - Part of Maxillary artery	
2nd arch	Regress-Stapedial a.	
3rd arch	L/R common, internal, and external carotid aa.	
4th arch	Part of Aortic Arch	Part of rt subclavian a.
6th arch	Left Pulmonary a. Ductus Arteriosus	Right Pulmonary a.
7th seg. a.	Left subclavian a.	Part of rt subclavian a.
Dorsal aorta	Descending thoracic aorta	Regress Part of rt subclavian a.

Vitelline and Umbilical Arteries

- **Vitelline Arteries :**
  - **I**nitially, a no. of paired vessels supplying the yolk sac .
  - Gradually fuse and form the arteries in the dorsal mesentery of the gut.
  - In adults, they fuse and form the **Coeliac, SMA and IMA** supplying foregut, midgut and hindgut respectively.
- **Umbilical Arteries :**
  - Initially paired ventral branches of the aorta
  - By 4th week, they acquire a secondary connection with the aorta and forms the common iliac artery
  - After birth, the proximal part persist as the internal iliac and superior vesical and the distal part obliterate to form the medial umbilical ligaments.

Coronary Arteries

- Derived From 2 Sources:
  1. **Angioblasts** – formed elsewhere and distributed over the heart surface by migration of the proepicardial cells

  2. The **Epicardium** itself.

- Some epicardial cells undergo an **epithelial-to-mesenchymal transition** induced by the underlying myocardium forming **endothelial and smooth muscle cells** of the coronary arteries.

- **Neural crest cells** also contribute smooth muscle cells along the proximal segments of these arteries.

- Connection to the aorta occurs by ingrowth of arterial endothelial cells from the arteries into the aorta.

Arterial system defects

- Patent ductus arteriosus
- Coarctation of the aorta (preductal and post ductal)
- Abnormal origin of the right subclavian artery
- Right aortic arch
- Interrupted aortic arch

Coarctation of the aorta

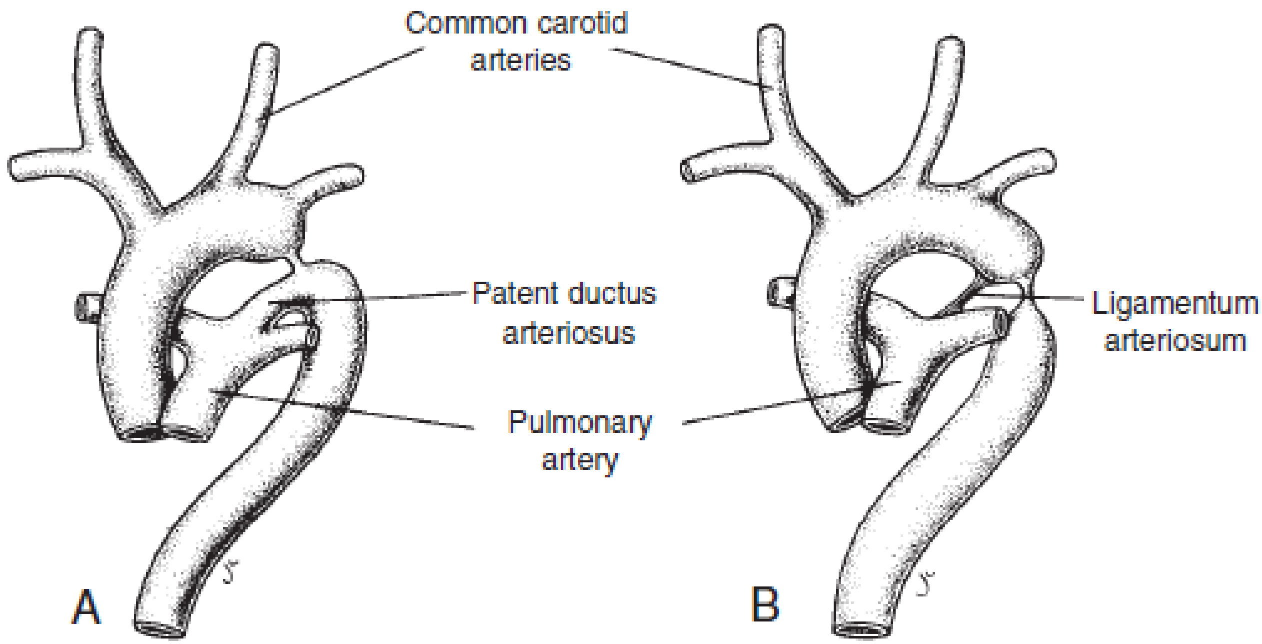


Figure 11.37 Coarctation of the aorta. **A.** Preductal type. **B.** Postductal type. The caudal part of the body is supplied by large hypertrophied intercostal and internal thoracic arteries.

Abnormal origin of the right subclavian artery

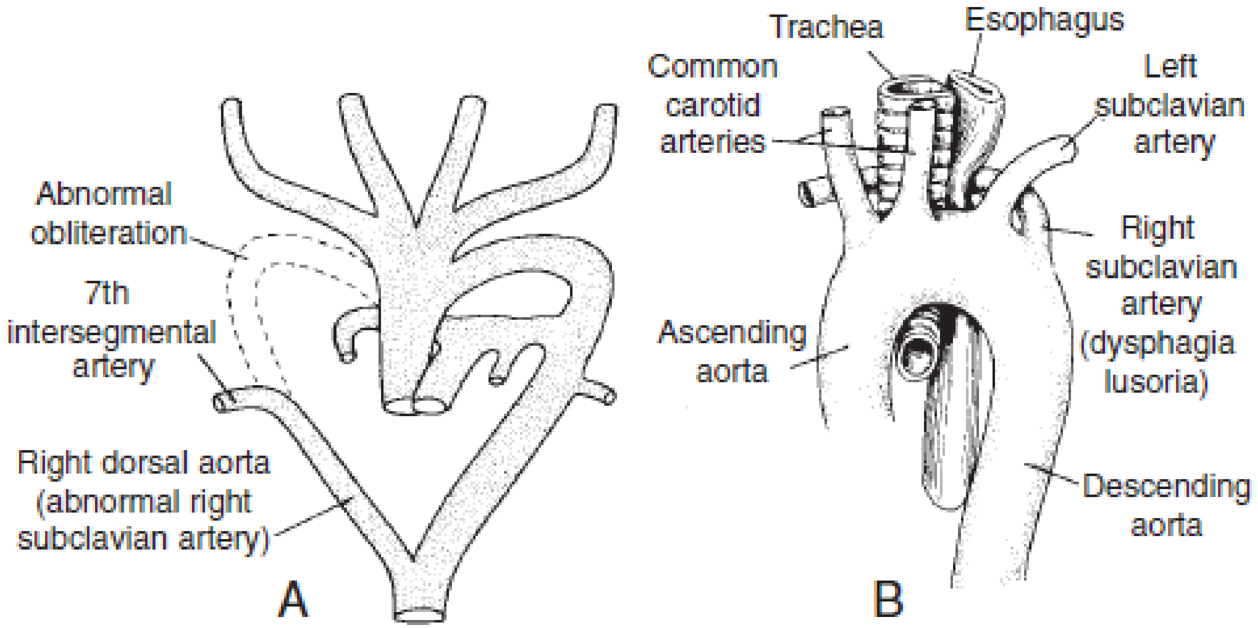


Figure 11.38 Abnormal origin of the right subclavian artery. **A.** Obliteration of the right fourth aortic arch and the proximal portion of the right dorsal aorta with persistence of the distal portion of the right dorsal aorta. **B.** The abnormal right subclavian artery crosses the midline behind the esophagus and may compress it.

Double aortic arch

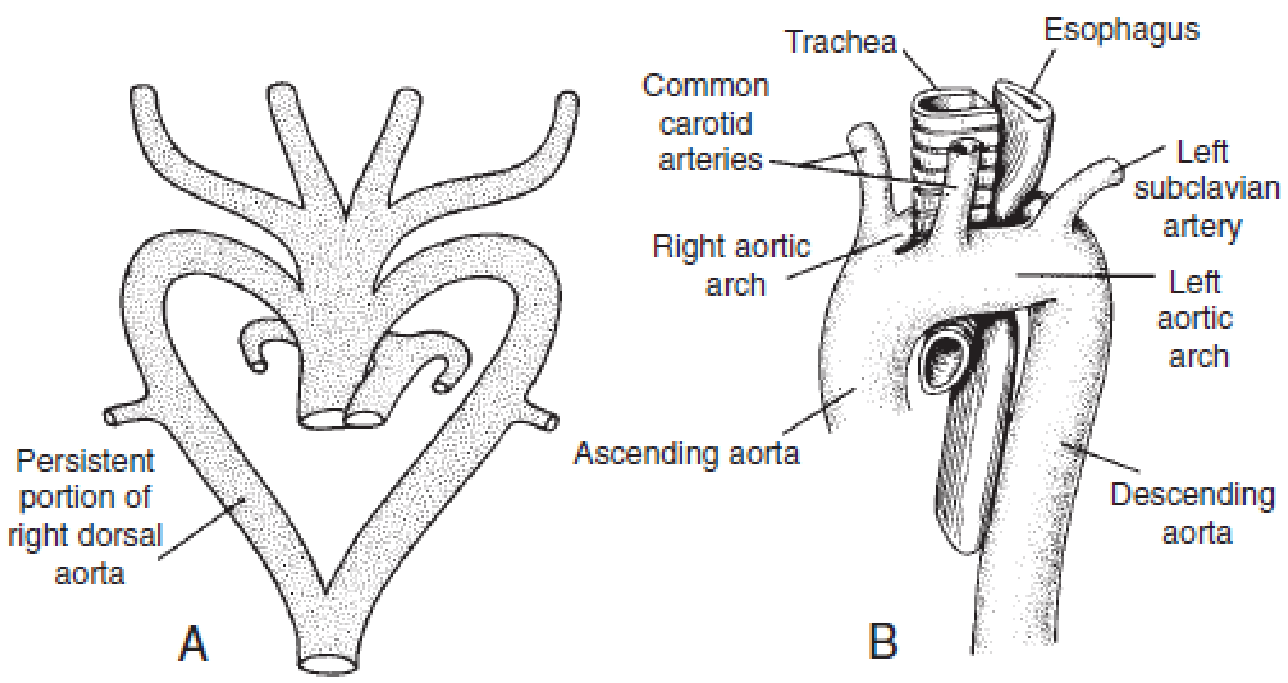


Figure 11.39 Double aortic arch. **A.** Persistence of the distal portion of the right dorsal aorta. **B.** The double aortic arch forms a vascular ring around the trachea and esophagus.

Interrupted aortic arch

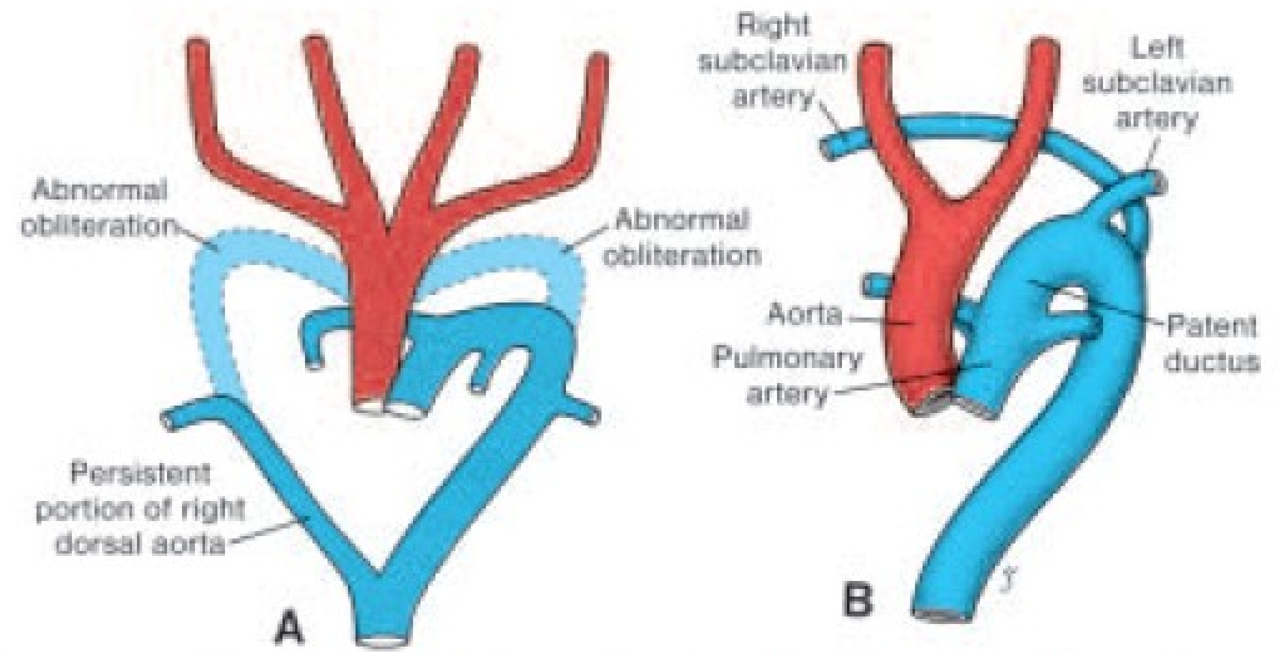
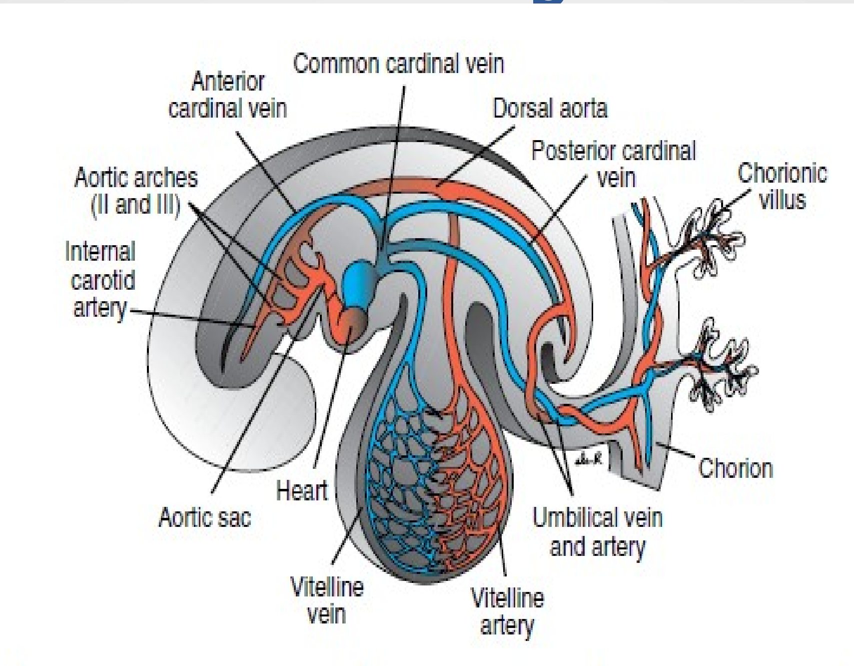


Figure 11.40 A. Obliteration of the fourth aortic arch on the right and left and persistence of the distal portion of the right dorsal aorta. **B.** Case of interrupted aortic arch. The aorta supplies the head; the pulmonary artery, by way of the ductus arteriosus, supplies the rest of the body.

Venous System



- In the **5th week**, three pairs of major veins can be distinguished:

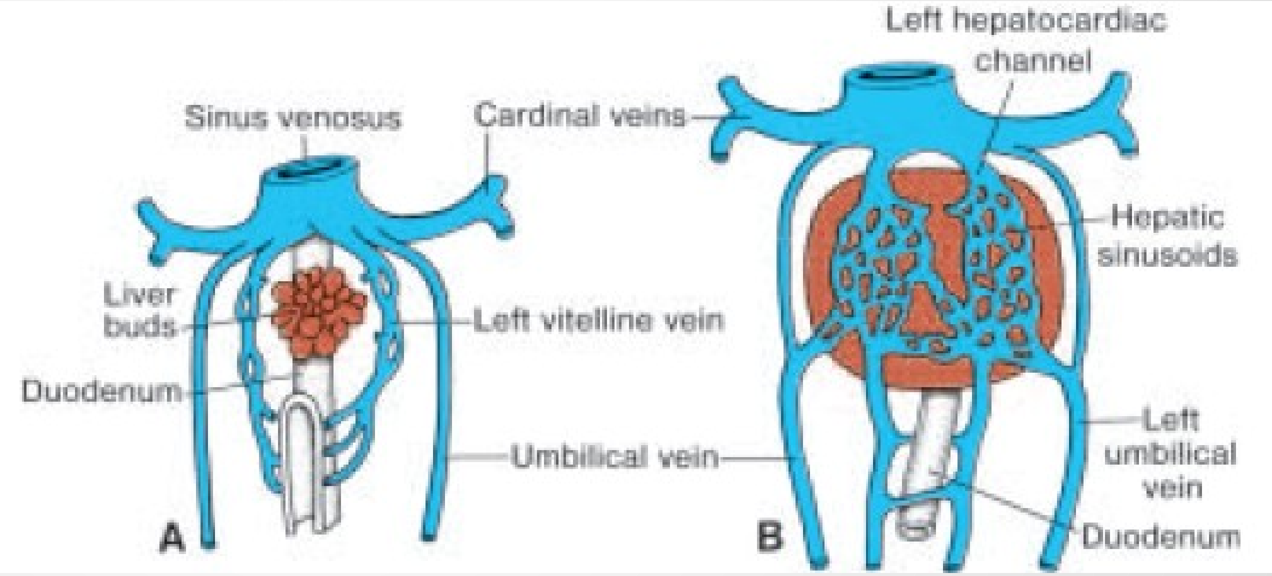
  1. Vitelline or Omphalomesenteric veins – carry blood from yolk sac to sinus venosus

  2. Umbilical veins – carry oxygenated blood to the embryo;

  3. Cardinal veins – draining the body of the embryo proper

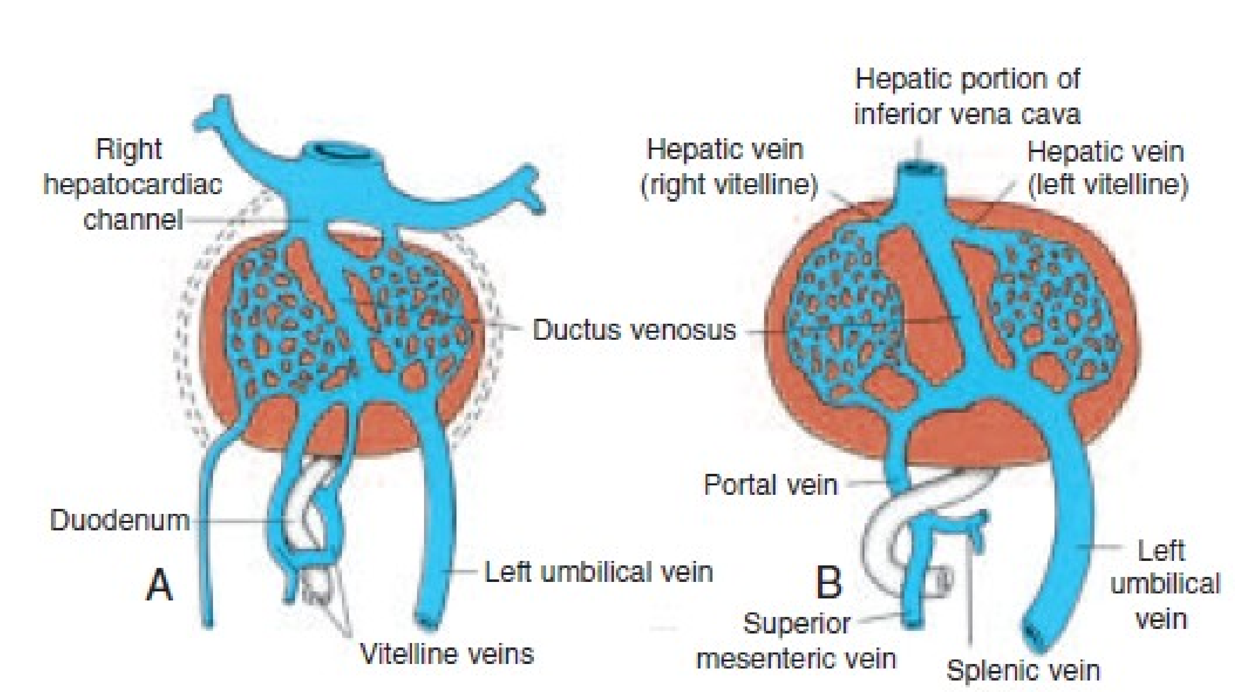
Vitelline Veins

- Forms a plexus around the duodenum, forms the **portal vein**.
- Pass through the **septum transversum**
- Hepatic cords grow into the septum and form the **hepatic sinusoids**
- Connects to the sinus venosum



Vitelline Veins

- Enlargement of the right vitelline vein.
- Forms **the hepatic cardiac part of the IVC**
- The SMV derives from the right vitelline vein
- The left vitelline vein disappears.



Umbilical veins

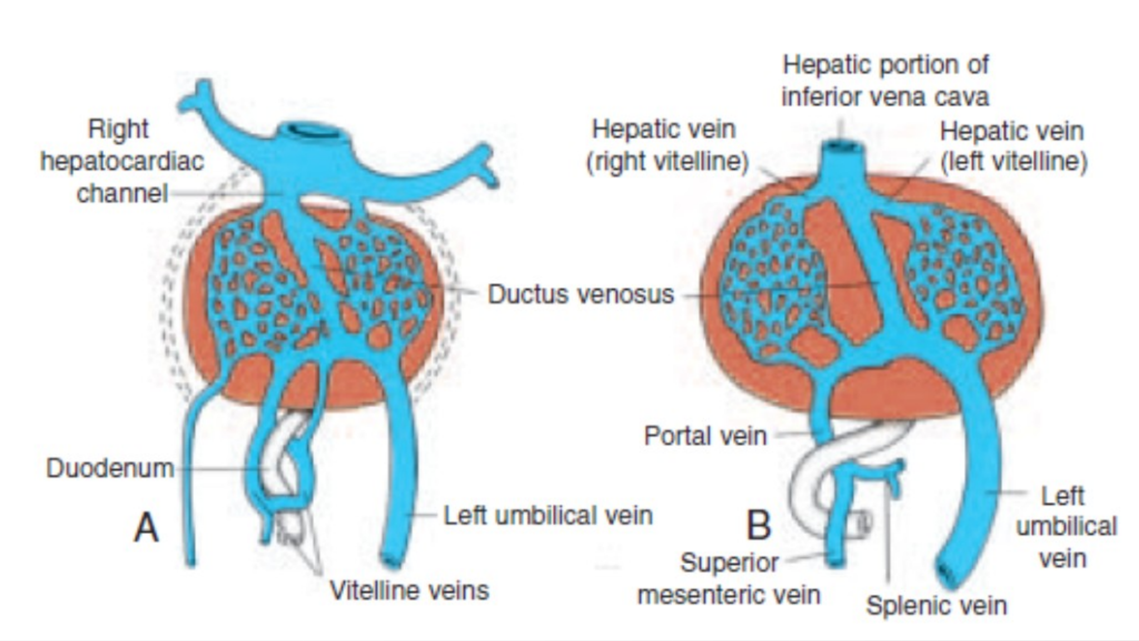
- Proximal and distal **right umbilical vein disappears**

- **Proximal left umbilical vein disappears**

- The **distal left umbilical vein** remains and carry blood from the placenta to the liver

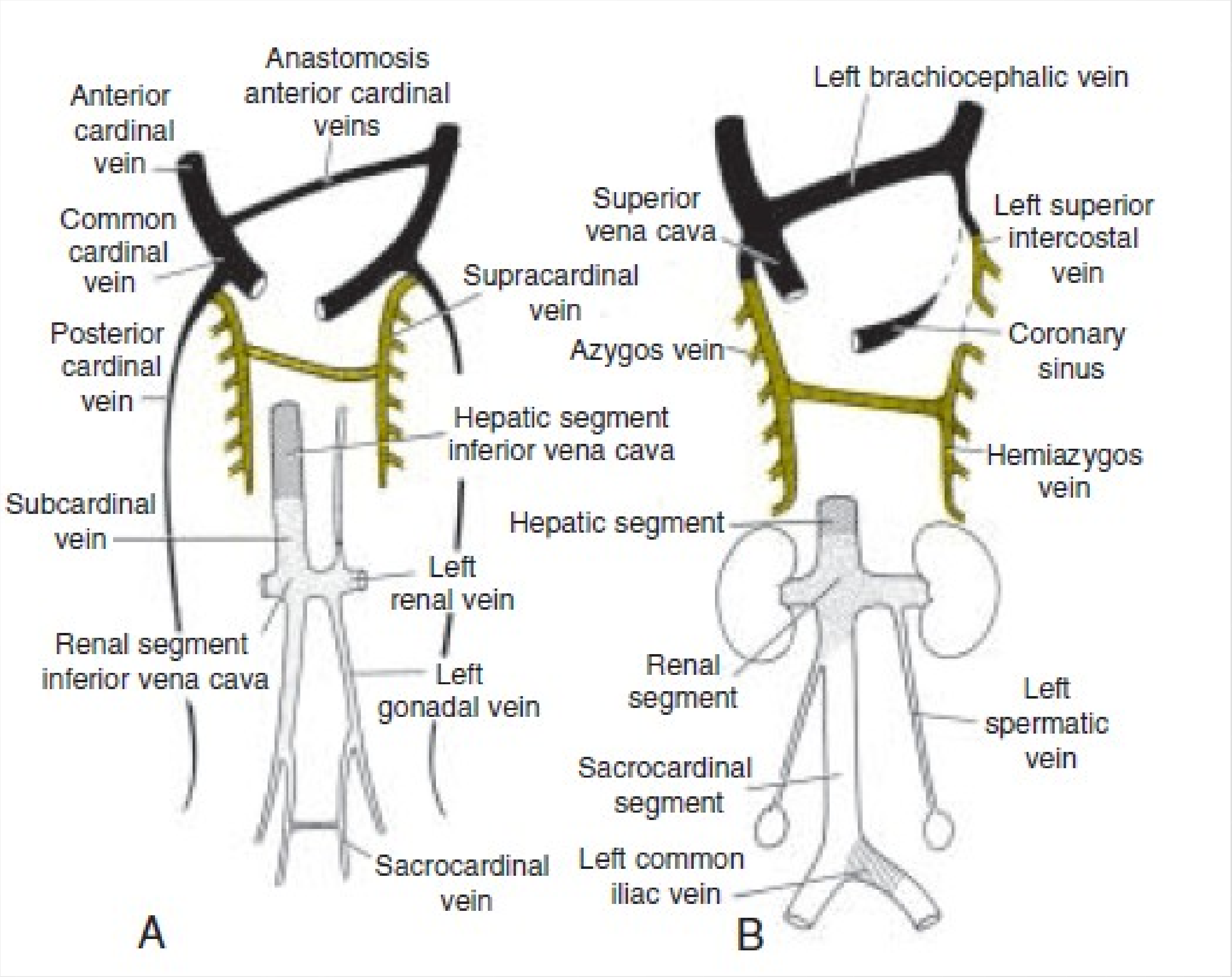
- The **ductus venosus** form between the left umbilical vein and right hepatic cardiac channel, it bypasses the sinusoidal plexus

- Both are obliterated after birth to form the **ligamentum teres and**



Cardinal Veins

- During the **4th week** this forms a symmetrical system.
- **Anterior cardinal veins,** drain the cephalic part of the embryo
- **Posterior cardinal veins,** drain the rest of the embryo.
- Both join to form **Common cardinal veins.**

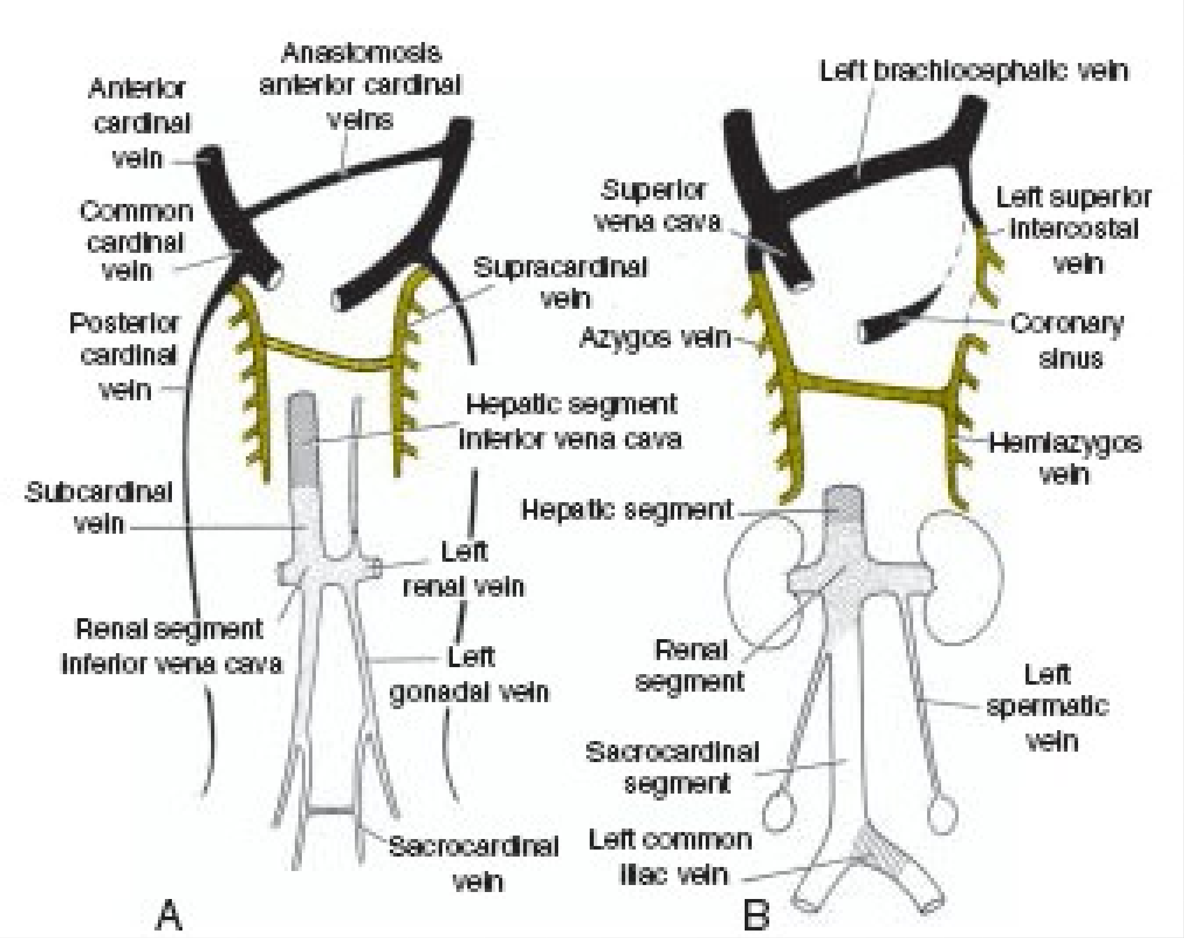


From the **5th-7th week** additional veins are formed:

a) Subcardinal veins, which mainly drain the kidneys;

b) **Sacrocardinal veins,** which drain the lower extremities;

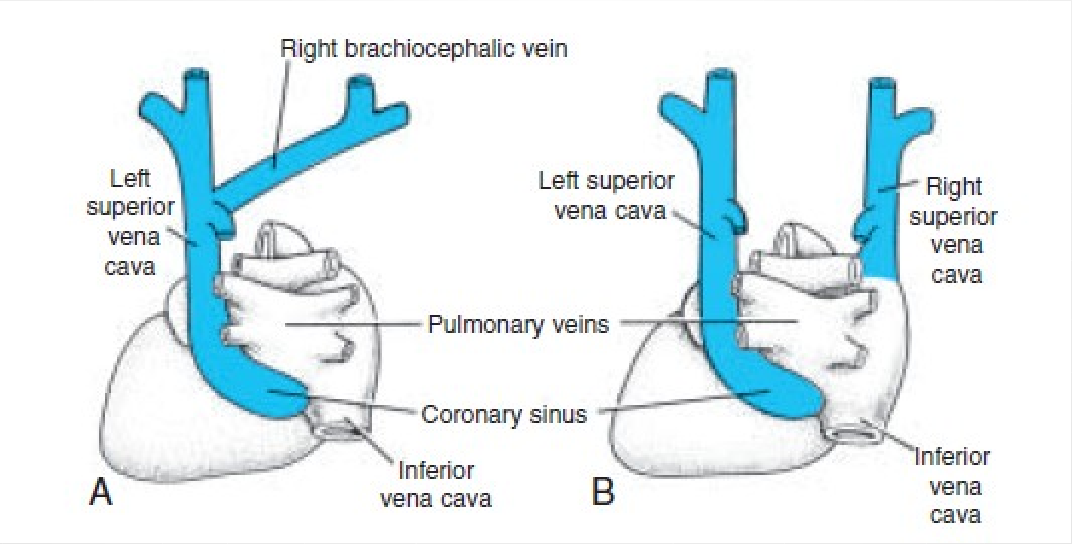
c) Supracardinalveins, which drain the body wall by way of the intercostal veins, taking over the functions of the posterior cardinal veins



Clinical correlates of Venous system defects

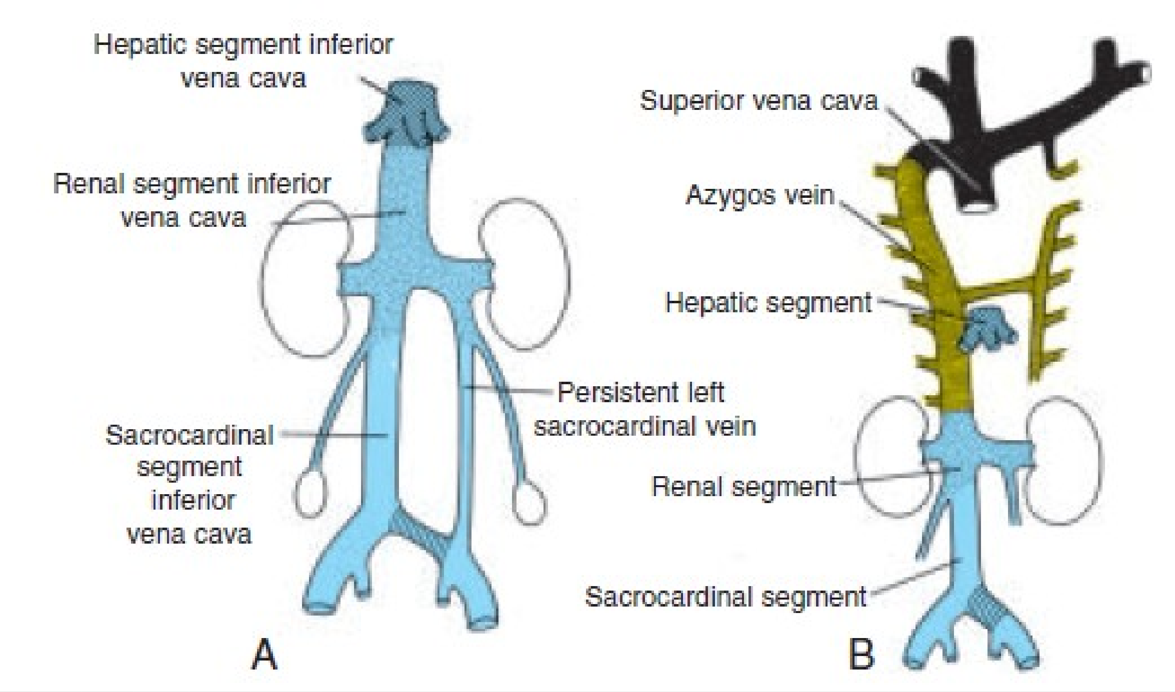
Left superior vena cava: Persistence of the left anterior cardinal vein
Obliteration of the common cardinal and anterior cardinal veins on the right

Double superior vena cava: Persistence of the left anterior cardinal vein
Failure of the brachiocephalic vein to form



Clinical correlates

- **Double inferior vena cava** : Left sacrocardinal vein remain connected to the left subcardinal vein
- **Absence of the inferior cava** : The right subcardinal vein fails to make the connection with the liver



THANK YOU